

Pollution Prevention (P2) Framework

**U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics**

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The models presented in OPPT's P2 Framework have been developed over a period of more than 20 years by OPPT, EPA contractors and/or grantees or others in the scientific and technical community, to screen chemicals in the absence of data. Through the P2 Framework, OPPT is presenting these screening models to industry and other stakeholders in the hopes that use of these models early in the research and development process will result in safer chemicals entering commerce. The P2 Framework models should be used to provide additional information on chemicals of concern.

Other chemical screening methodologies have been developed and are in use by chemical companies and other stakeholders. The Agency recognizes that other models are available and that these models can also be of value in chemical screening efforts.

CAUTION: Screening models provide estimations with an inherent degree of uncertainty, and should *never* be used to replace measured data from well designed studies. Measured data are always preferred over predicted data. If measured data are not available, measured data on close analogs can be used. If no analog data are available, screening level models, such as those in the P2 Framework, may be used to predict values that can be used to indicate which chemicals may need further testing.

NOTE: The URLs of certain Internet sites are provided as a convenience to users of the manual. Users are cautioned that due to the dynamic nature of the Internet, these URLs may have been changed from the time of the writing of this document. In case a URL is no longer correct, the user is advised to use any of the search engines to locate the correct URL.

NOTE: This document can be downloaded in PDF format from the Internet at
<http://www.epa.gov/oppt/p2framework/docs/p2manua.htm>

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Executive Summary

Publicly Available Data to Predict Chemical Risk are Often Lacking

Of the approximately 80,000 chemicals used in commerce in the United States, few have been tested, and only a fraction have sufficient publicly available data to allow a thorough evaluation of risk. Businesses, governmental organizations, and other stakeholders often don't have the data necessary to identify problem chemicals or identify safer substitutes or other options that are less risky, prevent pollution, and may save companies environmental management costs. At times, companies must make product and process decisions without enough data regarding the risk tradeoffs.

OPPT Screening Methods to Predict Risk-Related Information

The Office of Pollution Prevention and Toxics (OPPT) has developed computer-based methods that derive important risk assessment information based on chemical structure, conservative defaults, standard scenarios, and other factors. These methods provide information on physical / chemical properties, environmental fate, potential carcinogenicity, toxicity to aquatic organisms, worker and general population exposures, among other data. OPPT routinely uses these methods to highlight chemicals of concern, to identify safer substitutes, and to reduce or eliminate risks.

P2 Framework – a Compilation of OPPT Screening Methods

The Pollution Prevention Framework (“P2 Framework”) is compilation of many of OPPT's most important computer-based methods for predicting risk-related information. The P2 Framework provides important methods to predict risk-related information that may not be readily available. Its purpose is to provide information that can inform decision making and help promote the design, development, and application of safer chemicals, products, and processes. The document describes each methodology and the importance of the data generated, and provides case studies showing how methods can be used collectively to answer complicated risk assessment questions and identify pollution prevention opportunities. The P2 Framework, as currently constructed, does not address all biological endpoints. It is a set of screening-level methods that are of most value when chemical-specific data are lacking.

Sustainable Futures Initiative

Sustainable Futures is the programmatic structure OPPT developed to scale-up the successful P2 Framework-based Kodak and PPG Project XLs, and is designed to help industry develop new chemicals that are sustainable economically and environmentally. OPPT published a Federal Register notice announcing Sustainable Futures on December 11, 2002. The FR Notice is available at www.epa.gov/fedrgstr/EPA-TOX/2002/December/Day-11/t31243.pdf. Sustainable Futures offers industry an integrated path to the development of safer chemicals. This path includes: (1) comprehensive training in the use of the P2 Framework models, (2) specialized technical assistance within each industry sector, and (3) a Small Business Assistance Program, and (4) strong incentives.

Incentives

OPPT is offering regulatory flexibility to companies that participate in Sustainable Futures, allowing qualifying chemicals to be manufactured in 45 days, rather than the current 90-day structure. This is a powerful incentive for many companies. In addition to getting to market sooner, regulatory uncertainty is greatly reduced because the P2 Framework helps anticipate, and engineer away from, chemicals of concern. This is P2 in its purest form. In addition, use of the P2 Framework reduces product development and manufacturing costs.

Pollution Prevention and the Risk Assessment Process

What Is Pollution Prevention (P2)?

"Pollution Prevention", or "P2" is the common sense understanding that it is easier to prevent problems than to correct them. Congress, by enacting the Pollution Prevention Act of 1990 (42 U.S.C. 13101 and 13102, s/s et seq.), created a bold national objective for environmental protection by outlining a hierarchy in dealing with pollution:

- ❖ Pollution should be prevented or reduced at the source whenever feasible;
- ❖ Pollution that cannot be prevented should be recycled in an environmentally safe manner whenever feasible;
- ❖ Pollution that cannot be prevented or recycled should be treated in an environmentally safe manner whenever feasible; and
- ❖ Disposal or other releases into the environment should be employed only as a last resort and should be conducted in an environmentally safe manner.

Pollution prevention means "source reduction," as defined under the Pollution Prevention Act. The Pollution Prevention Act defines "source reduction" to mean any practice which:

- ❖ Reduces the amount of any hazardous substance, pollutant, or contaminant entering any waste stream or otherwise released into the environment prior to recycling, treatment, or disposal; and
- ❖ Reduces the hazards to public health and the environment associated with the release of such substances, pollutants, or contaminants.

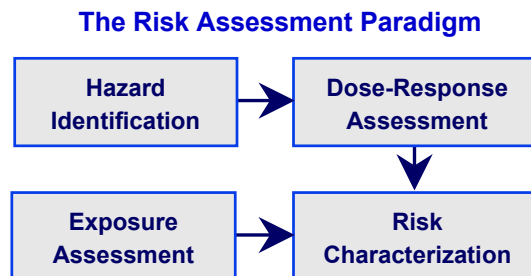
Source reduction can be achieved through equipment or technology modifications, processes or procedure modification, reformulation or redesign of products, substitution of materials, etc.

The Risk Assessment Process

In 1983, the National Academy of Sciences developed a 4 step paradigm for risk assessment and risk management*:

- ❖ **Hazard Identification:** Examining toxicity data to determine effects of a chemical on health of humans or other organisms (for example, increased cancer cases or birth defects);
- ❖ **Dose-Response Assessment:** Extrapolating toxicity data from high dose studies to predict the likely effect of low doses of the chemical (also referred to as Hazard Characterization);
- ❖ **Exposure Assessment:** Magnitude, frequency, and duration of exposure to a chemical (for example, exposures from proposed or actual manufacture, use, or disposal of a chemical); and
- ❖ **Risk Characterization:** Estimates potential for, and magnitude of, risk to an exposed individual or population.

The components of the risk assessment process are illustrated in the figure below.



*NRC. 1983. Risk Assessment in the Federal Government: Managing the Process. National Research Council. National Academy Press, Washington, DC. ISBN: 0-309-03349-7.

Risk Information Improves Decision Making

Understanding the Problem is Key to Identifying P2 Opportunities and Sustainability

Each year industry develops new chemical substances, substances previously unknown to commerce. The Toxic Substances Control Act (TSCA) gives EPA authority to regulate new chemicals, i.e., chemicals not already listed on the TSCA Inventory. For help determining if a chemical substance is on the TSCA Inventory go to <http://www.epa.gov/opptintr/newchems/invntory.htm>. EPA's regulatory authority to regulate new chemicals is described under the PreManufacture Notice (PMN) Provisions of TSCA. Before manufacture for commercial purposes, industry must submit a PMN to EPA, and EPA, OPPT has 90 days to identify chemicals posing risk(s) and regulate when needed. There is no requirement under TSCA that the submitter conduct testing on new chemicals, however if tests are conducted, this data must be submitted with the PMN. Less than 10% of PMNs submitted have publicly available data such as an LD50. An alarmingly small number of PMNs have enough publicly available data to perform a rudimentary assessment of risk.

Uncertain Risks

Industry submits 2,000 PMNs annually. In many cases, when alternative chemicals or processes are considered at R&D, commercialization decisions are based on factors such as efficacy, yield, performance, and cost. While EPA sees 2,000 PMNs per year, industry has made thousands of other decisions early in R&D, long before PMN submission. By the time EPA sees the PMN, most of the P2 opportunities have been lost. Industry has needed to make decisions without understanding risk tradeoffs of product/process alternatives.

Risk-Related Information is Needed to Take Advantage of P2 Opportunities

To identify and take advantage of pollution prevention opportunities, stakeholders need access to risk-related information. Companies often decide which chemicals or processes to use primarily on the basis of cost and product performance, among other criteria. If companies had access to risk-related information about chemicals, they could improve decision making and take advantage of pollution prevention opportunities.

Technology Provides an Opportunity

Faced with tight statutory deadlines (90 days) and the absence of hazard/risk data, OPPT turned to technology to fulfill its mission. Working with others in the scientific community, OPPT developed risk screening methods that use SARs - Structure Activity Relationships. The SAR approach calculates or infers hazard, exposure and risk issues based on an analysis of chemical structure. SAR techniques include computational toxicology, expert systems, among other approaches. Endpoints addressed include, environmental fate, cancer hazard, aquatic toxicity, exposure, and risk among other factors. OPPT has computerized many of these methods and uses these to evaluate PMNs and existing chemicals where data are lacking. OPPT has over 20 years of experience in this area.

P2 Framework

The P2 Framework is a compilation of some of OPPT's most important methods for assessing hazard and risk when chemical specific data are lacking. This **P2 Framework Manual** describes each methodology contained in the P2 Framework and how the predictions generated can be used in decision making. This document also includes case studies showing how the methods can be used collectively to answer complicated risk assessment questions and identify P2 opportunities. The P2 Framework can provide important risk-related information that may not be available elsewhere. The purpose of the P2 Framework is to help identify pollution prevention opportunities by providing information that can inform decision making and help promote the design, development and application of safer chemicals and processes.

Risk Information Improves Decision Making

P2 Framework Methods Provide Screening Level Risk-Related Information

Most methods presented in OPPT's P2 Framework deal with two steps of the risk assessment process: hazard identification and exposure assessment. Ideally, information on the potential hazards posed by a chemical as well as exposure information will be available, but often this is not the case. Methods included in the P2 Framework are intended to provide screening level information to help in assessing potential risk posed by a chemical or group of chemicals.

What to Do When There Are No Data

The methods are intended to be used when data are unavailable or to supplement available data. These methods are generally computer models that assess a particular aspect of a chemical's possible impact on humans or the environment. For example, one model estimates toxicity to fish, aquatic invertebrates, and algae. This is important information if the chemical is or will be discharged to streams during manufacture, processing, use, or disposal. The OncoLogic model estimates the likelihood that a chemical would cause cancer in humans. Other models estimate potential exposures to a chemical in consumer products. Models are also presented for estimating properties such as vapor pressure and water solubility, which are important for projecting the nature, magnitude, and duration of exposure.

P2 Framework Outreach

OPPT wanted to learn if its SAR techniques could be transferred to industry and if these methods could be used early in R&D to evaluate PMN product alternatives based on risk. OPPT integrated these methods into a program called the Pollution Prevention Framework (P2 Framework), a science-based analytical framework for identifying safer new chemicals. OPPT developed P2 Partnerships with many industry sectors to help them explore the application of the P2 Framework methods to their chemicals of interest.

Summary of Kodak and PPG XL Projects

OPPT's outreach efforts to industry on the P2 Framework have been highly successful and formed the basis of two Project XLs with Kodak and PPG Industries. PPG and Kodak facilities are using the P2 Framework to screen all materials being considered for submission to EPA as new chemicals. Both companies will use the P2 Framework during the early stages of product development, allowing them to improve the environmental performance of products while reducing costs, saving time, enhancing competitive advantage and decreasing potential liability. Under the XL project, PPG verified the accuracy of the P2 Framework by comparing actual toxicity studies on 38 polymers with estimates from the P2 Framework with agreement between the two being 87- 90%. Kodak conducted an analysis of the economic and business benefits of application of the P2 Framework, and found that using the P2 Framework helped identify environmentally preferable products, lowered product development costs, reduced time to market and lowered full-scale manufacturing costs.

These Methods Provide Information in Four Areas

The P2 Framework models provide information in the following areas:

Physical/Chemical Properties

- ❖ Melting point
- ❖ Boiling point
- ❖ Vapor pressure
- ❖ Water solubility
- ❖ Henry's law constant
- ❖ Soil organic carbon adsorption

Hazard to Humans and the Environment

- ❖ Carcinogenicity potential
- ❖ Aquatic toxicity
- ❖ Non-cancer human health effects

Chemical Fate in the Environment

- ❖ Atmospheric oxidation potential
- ❖ Hydrolysis
- ❖ Biodegradation
- ❖ Bioconcentration and bioaccumulation
- ❖ Percent removal in wastewater treatment
- ❖ Percent in each media
- ❖ Persistence

Exposure and/or Risk

- ❖ Consumer dermal exposure
- ❖ Consumer inhalation exposure
- ❖ CC exceedences from discharges to surface water
- ❖ Workplace releases and exposures

The P2 Framework is set of screening-level methodologies that can be used when chemical-specific data are lacking. **If data are available for a given endpoint from a well conducted test, they should be used instead of data generated by the P2 Framework models or similar screening-level models.** Some methods included in the P2 Framework provide quantitative estimates (e.g., methods to estimate aquatic toxicity), while others, such as the OncoLogic model, provide qualitative hazard estimates. The computerized models in the P2 Framework do not address all human health effects. For this reason EPA has included a protocol that may be useful for screening chemicals for non-cancer human health effects.

Sustainable Futures Initiative – Regulatory Relief for Low Hazard/Low Risk New Chemical Substances

Sustainable Futures Initiative

Sustainable Futures (www.epa.gov/opptintr/newchems/sustainablefutures.htm) is the programmatic structure OPPT developed to scale-up the P2 Framework-based Kodak and PPG XLs (<http://www.epa.gov/projectxl/>), and is designed to help industry develop new chemicals that are sustainable economically and environmentally. OPPT published a Federal Register notice announcing Sustainable Futures on December 11, 2002. The FR Notice is available at www.epa.gov/fedrgstr/EPA-TOX/2002/December/Day-11/t31243.pdf. Sustainable Futures offers industry an integrated path to safer chemicals, this path includes: (1) comprehensive P2 Framework training, (2) specialized technical assistance within each industry sector, and (3) a Small Business Assistance Program, and strong incentives.

Incentives

OPPT is offering regulatory flexibility to companies that participate in Sustainable Futures, allowing qualifying low hazard/low risk chemicals to be manufactured in 45 days, rather than the current 90-day structure. This is a powerful incentive for many companies. In addition to getting to market sooner, regulatory uncertainty is greatly reduced because the P2 Framework helps anticipate, and engineer away from, chemicals of concern. This is P2 in its purest form. In addition, use of the P2 Framework reduces product development and manufacturing costs.

What Must Submitters Do to Qualify for Expedited PMN Review?

In order to qualify for this pilot project, and associated expedited review, companies subject to TSCA section 5 reporting requirements must demonstrate experience and competence with the P2 Framework or other scientifically acceptable approaches to chemical risk screening. In order to do this, companies will need to:

1. Take training in the use of risk screening models such as the P2 Framework and PBT Profiler. EPA sponsored training is listed at www.epa.gov/opptintr/newchems/sustainablefutures.htm
2. Apply hazard and exposure screening tools and demonstrate to EPA that this information has been used to inform decision making to select safer new chemical alternatives to submit as new chemical notifications (and, where appropriate, to identify opportunities to eliminate or control exposures through process controls); and
3. Submit 5-10 successful (i.e., not regulated by EPA) PMNs or PMN exemption notices which have been developed using chemical hazard and exposure screening tools. These submissions should also include documentation of chemicals evaluated, models used, endpoints on which decisions were based, and the submitter's perspectives on the extent to which the screening tools provided useful information to compare alternatives and select safer chemicals.

The Risk Standard Is Not Lowered

OPPT will continue to conduct an independent risk evaluation of each PMN submitted, and those that EPA finds to be low hazard/low risk qualify for relief. EPA makes this determination in the first 30 days of the 90-day review period. Chemicals that do not make the low hazard/low risk cut in the first 30 days won't qualify for relief. As a result, there will be no lowering of the risk standard.

Win-Win-Win

Under Sustainable Futures industry wins by getting to market sooner, reducing regulatory uncertainty, and lowering development/production costs. The environment wins because inherently safer chemicals and processes are commercialized. EPA wins by advancing key P2 and risk reduction goals and objectives.

P2 Framework Models

Model	Input	Output
Models to Estimate Physical / Chemical Properties		
MPBPVP™	CAS RN or Chem. Str. in SMILES	MP, BP, VP
WSKOWWIN™	CAS RN or Chem. Str. in SMILES	Water solubility from log KOW
KOWWIN™	CAS RN or Chem. Str. in SMILES	Octanol / water partition coefficient
HENRYWIN™	CAS RN or Chem. Str. in SMILES	Henry's law constant: VP/WS
PCKOCWIN™	CAS RN or Chem. Str. in SMILES	Soil organic carbon partition coefficient
Models to Estimate Chemical Fate in the Environment		
AOPWIN™	CAS RN or Chem. Str. in SMILES	Atmospheric oxidation potential
HYDROWIN™	CAS RN or Chem. Str. in SMILES	Hydrolysis rate
BIOWIN™	CAS RN or Chem. Str. in SMILES	Biodegradation potential
BCFWIN™	CAS RN or Chem. Str. in SMILES	Bioconcentration factor
STPWIN™	CAS RN or Chem. Str. in SMILES	Percent removal in POTW
LEV3EPI™	CAS RN or Chem. Str. in SMILES	Percent in each medium
Models to Estimate Hazards to Humans and the Environment		
OncoLogic	Chemical structure	Cancer hazard potential
ECOSAR	CAS RN or Chemical Structure in SMILES, if available measured WS, LogKow, MP	Acute and Chronic toxicity to fish, invertebrates, algae, SAR chemical class
PBT Profiler	CAS No. or Chemical structure drawn or in SMILES	<u>Persistence</u> : media half-lives and percent in each medium; <u>Bioaccumulation</u> : fish BCF; <u>Toxicity</u> : fish chronic toxicity and identification of structures known to have human health concerns.
Models to Estimate Exposure and / or Risk		
E-FAST	Physical / chemical properties, fate properties, release amounts, release medium, release location, aquatic concentration of concern, NPDES number	Surface water ingestion, fish ingestion, ground water ingestion, ambient air inhalation, indoor air inhalation, dermal exposure, exposure/risk to aquatic environment
ChemSTEER	Production or assessed volume (kg chemical per year); chemical properties and workplace mass balance (when known); uses and workplaces to be assessed; % volume to each workplace; sources and activities with chemical releases and worker exposures	Media of release; number of sites; days of release per medium (days/site-year); daily & annual release rates (kg/site-day & kg/year – all sites); Worker inhalation & dermal doses (mg/day & mg/kg/day) ; numbers of workers exposed

What is Required to Use the P2 Framework Models?

Essential Information

All of the tools require minimal, but important information. For example, physical and chemical properties such as molecular weight are important. Other models require the user to input the amount of chemical likely to be discharged to a stream or river. The table on the following page summarizes the required input information as well as the output data for each model.

Knowledge or Expertise Required

Knowledge needed will vary depending on the application. For example, the models KOWWIN and PCKOCWIN only require chemical structure or CAS Number; however, ECOSAR and OncoLogic require that the user have a good understanding of organic chemistry. The Screening for Non-cancer Human Health Effects protocol should be by an experienced human health toxicologist. User's Guides and technical assistance are available to help when you are uncertain how to proceed.

Computer Requirements

These models are designed to run on IBM compatible personal computers. The specific computer requirements (memory and disk size) necessary to run each of these models vary and are provided on the following page.

Model Availability

Models to Estimate Physical/Chemical Properties of Chemicals:

MPBPVP™, WSKOWWIN™, KOWWIN™, HENRYWIN™ methods, incorporated into the EPI Suite™, were developed by Syracuse Research Corporation (SRC) for US EPA, OPPT and can be downloaded from www.epa.gov/opptintr/exposure/docs/EPI_Suitedl.htm

Models to Estimate Chemical Fate in the Environment:

AOPWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, LEV3EPI™ incorporated into the EPI Suite™, were developed by SRC for US EPA, OPPT and can be downloaded from www.epa.gov/opptintr/exposure/docs/EPI_Suitedl.htm

The LEV3EPI™ fugacity model is based on Level III Fugacity model developed by Don Mackay of Trent University (www.trentu.ca/cemc/VBL3D.html). LEV3EPI has been incorporated into the EPI Suite™ and can be downloaded from the Internet at: www.epa.gov/opptintr/exposure/docs/EPI_Suitedl.htm.

Models to Estimate Hazard to Humans and the Environment:

OncoLogic, developed by LogiChem under a cooperative agreement with USEPA, OPPT in support of Sec. 5 of TSCA, can be obtained by contacting: Marilyn S. Arnott, Ph.D., LogiChem, Inc., PO Box 622, Narberth, PA 19072, Email: marnott@ptdprolog.net
ECOSAR can be downloaded from the Internet at: www.epa.gov/oppt/newchems/21ecosar.htm or by contacting Vince Nabholz, EPA, OPPT at nabholz.joe@epa.gov

Model to Estimate Persistence, Bioaccumulation, and Toxicity

The PBT Profiler screening model was developed by SRC for OPPT to help users prioritize chemicals based on their potential to persist, bioaccumulate, and be toxic. The PBT Profiler can be accessed on the Internet at www.pbtprofiler.net.

Modes to Estimate Exposure and/or Risk:

The E-FAST Model and documentation manual can be downloaded at no cost from EPA's Internet site at: www.epa.gov/opptintr/exposure/docs/efast.htm
ChemSTEER can be downloaded at no cost from EPA's Internet site at: www.epa.gov/opptintr/exposure/docs/chemsteer.htm

Computer Requirements

Computer Requirements

The P2 Framework models are designed to run on IBM compatible personal computers. The specific computer requirements (memory and disk size) necessary to run each of these models vary and are provided below.

EPI Suite™ which includes MPBPVP™, WSKOWWIN™, KOWWIN™, HENRYWIN™, AOPWIN™, WVOLWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, and LEV3EPI™, requires:

- ❖ IBM-compatible PC with Microsoft Windows 3.1, 95, 98, 2000 and Windows NT
- ❖ 10 MB of hard disk space
- ❖ SMILECAS requires 10 MB of hard disk space
- ❖ LEV3EPI requires at least a 75MHz processor (adjustment of screen resolution may be necessary)

OncoLogic

- ❖ 386 PC with MS-DOS 5.0 or later,
- ❖ 570K of conventional RAM
- ❖ 60 megabytes of hard disk space
- ❖ A disk cache will significantly improve performance

ECOSAR

- ❖ IBM-compatible PC with a 640-KB memory
- ❖ 512-550 KB of free memory
- ❖ 80386 or 80286 processor
- ❖ MS Windows 3.1, 95, 98, or NT
- ❖ Expanded memory and disk cache will improve performance
- ❖ At least 51 file handlers specified in the CONFIG.SIS file

PBT Profiler

- ❖ Java-enabled web browser that is set to accept cookies

E-FAST

- ❖ IBM-compatible PC with a 640-KB memory
- ❖ 512-550 KB of free memory
- ❖ 80386 or 80286 processor
- ❖ MS Windows 3.1, 95, 98, or NT
- ❖ At least 51 file handlers specified in your CONFIG.SIS file
- ❖ An expanded memory and disk cache will improve performance

ChemSTEER

- ❖ IBM-compatible PC Pentium or higher processor (500 MHz or faster recommended)
- ❖ Monitor with 800 x 600 resolution or higher
- ❖ Windows 95 or higher
- ❖ 64 megabytes of memory
- ❖ 30 megabytes of hard disk space (installed files); 25 MB (installation file can be deleted following installation)

About This Document

Contents of This Document

This manual explains the models used by OPPT to screen potential exposures and risks posed by chemicals. Each model answers important questions about a chemical's potential impact on humans or the environment. The models are described in this document by briefly detailing the important information they provide. Flow diagrams presenting step-by-step use of some of the more complex models are also included. In addition, a series of structured examples (case studies) are provided to show how the models can answer specific environmental questions and how the models can be used in combination to answer complicated exposure/risk-related questions.

We believe this information will be useful to you. The manual provides some information on how to use the models. However, we recognize that you may still have questions after you read this material. Technical assistance is available from OPPT to answer those questions.

Users of This Document

You are reading this manual because you are interested in opportunities to prevent pollution. These opportunities may also decrease costs to your company or organization. As you read, please keep in mind that this version of the P2 Framework is the first step in an evolving process. All comments and suggestions for improvement are welcome. Please direct comments to:

Maggie Wilson, EPA, OPPT
Phone: 202-564-8924
Email: wilson.maggie@epa.gov

How This Document Is Organized

This document presents brief overviews of each model. Each overview provides enough information to successfully run each model. More detailed information on each model is provided in the User's Guide or supplemental documentation for that model.

A glossary of relevant terms is also included. Appendices include (1) Case Studies which illustrate how the models can be used in combination to answer complicated risk-related questions; (2) Data Sources to search for measured data; (3) and Summary of Writing SMILES notation.

P2 Framework Models

The models included in this manual are listed below, and are presented in the illustration on the following page. The illustration can be used as an informal “road map” to approximate the endpoints the model addresses and help decide which models you might wish to use.

PHYSICAL/CHEMICAL PROPERTY MODELS:

MPBPVP™, WSKOWIN™, KOWWIN™, HENRYWIN™

FATE MODELS:

AOPWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, LEV3EPI™

HAZARD MODELS:

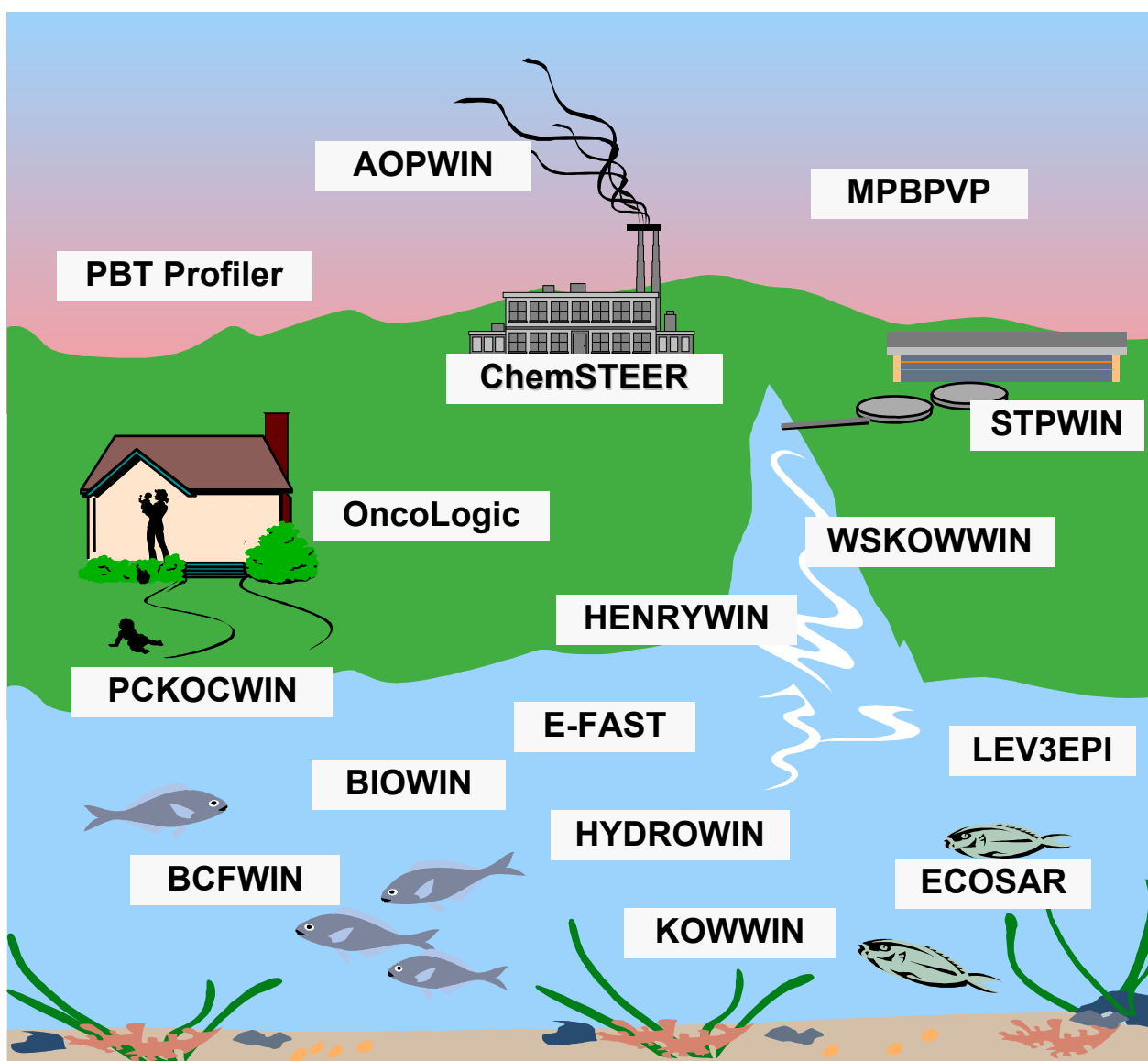
OncoLogic, ECOSAR

P, B, T POTENTIAL:

The PBT Profiler

EXPOSURE and/or RISK MODELS:

E-FAST, ChemSTEER



EPI Suite™ and SMILES

What Is EPI Suite™?

Estimations Programs Interface for Windows - EPI Suite™ - provides a quick and easy way to run the estimation programs, listed below, from a single entry for a single chemical. EPI Suite™ can sequentially run: AOPWIN™, BCFWIN™, BIOWIN™, ECOSAR, HENRYWIN™, HYDROWIN™, KOWWIN™, LEV3EPI™, MPBPVP™, PCKOCWIN™, STPWIN™ and WSKOWWIN™. The chemical structure or CAS Number is entered only once, and EPI Suite™ executes all of the programs in sequence and captures their output. Any of the estimation programs may be run separately. EPI Suite™ can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. The EPI Suite™ Programs also can input chemical structure formats generated by other computer programs. These importable formats include:

Alchemy III MOL files	HyperChem HIN files	PCModel files
Beilstein ROSDAL files	MDL ISIS SKC files	Softshell SCF files
BioCAD Catalyst TPL files	MDL MOL files	Tripos Sybyl Line Notation
ChemDraw files	Molecular Presentation	Tripos SYBYL MOL2 files
ChemDraw Connection Tables	Graphics (MPG) files	

EPI Suite™ Data Entry

To the right is the EPI Suite™ data entry page. A chemical is entered only once and EPI will run each of the estimation programs, listed above, and provide results from each program. Chemical structure can be entered using CAS RN, Smiles string, or imported from a chemical draw Program. Many good draw programs are available, such as ISIS Draw, which is available at no cost from MDL at www.mdli.com

What Is SMILES?

SMILES is "Simplified Molecular Input Line Entry System," which translates a chemical's structure

into a string of symbols that is easily understood by computer software. You can learn to write SMILES notations, as described in Appendix C. For all EPI Suite™ estimation programs, enter only the SMILES notation for the chemical, and the program provides the estimation you need.

Writing SMILES Notations

The SMILES notation system was designed by chemists for computer use (Weininger, 1988. J. Chem. Inf. Comput. Sci. 28: 31-6). SMILES notations depict the molecular structure of a chemical as a 2-dimensional picture. Learning to write a SMILES notation is not difficult, but it can be tricky. The same 3-dimensional structure can be written correctly using many different SMILES notations.

A summary of directions for writing SMILES notations is included in Appendix C of this document. Complete directions for writing SMILES notations are included in the EPI Suite™ User's Guide, and the Help files in each EPI Suite™ and the ECOSAR model include examples of SMILES notations.

The User's Guide for each model is available in the Help screens.

Models to Estimate Physical/Chemical Properties of Chemicals

The PHYSICAL/CHEMICAL PROPERTY MODELS included in this section are:

- ❖MPBPVP™
- ❖WSKOWWIN™
- ❖KOWWIN™
- ❖HENRYWIN™
- ❖WVOLWIN™
- ❖PCKOCWIN™

Following are brief fact sheets providing information on the models OPPT has developed and uses to estimate environmental fate of chemicals. Information provided on each model includes:

- ❖What physical/chemical property does the model estimate?
- ❖What is significant about the physical/chemical property to risk assessment?
- ❖Why is knowing physical/chemical properties important?
- ❖Why would I want to use the model?
- ❖What do I need to run the model?
- ❖What are the inputs and outputs for the model?

MPBPVP™ to Estimate Melting Point, Boiling Point, and Vapor Pressure

What Does the MPBPVP™ Model Do?

MPBPVP™ estimates an organic chemical's melting point, boiling point, and vapor pressure at 25 deg C using a combination of techniques.

How are the model predictions useful in risk assessment?

Melting Point (MP), the temperature at which a chemical changes from solid to liquid, gives clues to other chemical properties:

- ❖ MP indicates the state (solid-liquid-gas) of the chemical in the ambient environment.
- ❖ High MP indicates low water solubility.
- ❖ Low MP indicates increased absorption is possible through the skin, GI tract, or lungs.
- ❖ The range of measured MPs indicates its purity: narrow = more pure, wide = less pure.
- ❖ MP <100°C = increased volatility and higher potential exposures.

Boiling Point (BP), the temperature at which the VP of a chemical in a liquid state equals atmospheric pressure, gives clues to other chemical properties:

- ❖ High BP indicates low VP, for example structurally large substances like polymers.

Vapor Pressure (VP), the pressure at which a liquid and its vapor are in equilibrium at a given temperature, gives clues to other chemical properties:

- ❖ Chemicals with VP $\geq 10^{-4}$ mm Hg (higher VP) exist mostly in the vapor phase in the atmosphere, and often have higher potential inhalation exposures than chemicals with low vapor pressure.
- ❖ Chemicals with VP 10^{-5} to 10^{-7} mm Hg exist in both vapor and solids or particulate phases.
- ❖ Chemicals with (lower VP) $\leq 10^{-8}$ mm Hg exist mostly as solids.

Inputs Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Estimations of melting point, boiling point, and vapor pressure at 25 deg C
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of Melting Point, Boiling Point, and Vapor Pressure Values

Examples of Melting Points at 25 deg C

CAS RN	Chemical	Degrees C
60571	Dieldrin	135
108952	Phenol	-2
75092	Dichloromethane	-90
67641	Acetone	-94
50000	Formaldehyde	-111

Examples of Boiling Points at 25 deg C

CAS RN	Chemical	Degrees C
60571	Dieldrin	340
108952	Phenol	170
75092	Dichloromethane	80
67641	Acetone	45
50000	Formaldehyde	10

Examples of Vapor Pressures at 25 deg C

CAS RN	Chemical	Degrees C
60571	Dieldrin	1.77E-5
108952	Phenol	1
75092	Dichloromethane	86
67561	Methanol	396
50000	Formaldehyde	1330

Sample Output from the MPBPVP™ Model

Where Can I Get MPBPVP™?

MPBPVP™ v1.40 has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedl.htm. If you download and install EPI Suite™ you can run MPBPVP™ as a stand-alone model by putting a shortcut to the MPBPWIN.exe file on your Windows Desktop.

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

INPUTS: CAS Number 108883 (Methyl-benzene or toluene)

RESULTS:

Experimental Database Structure Match:

Name : TOLUENE
CAS Num : 000108-88-3
Exp MP (deg C): -94.9
Exp BP (deg C): 110.6
Exp VP (mm Hg): 2.84E+01
Exp VP (deg C): 25
Exp VP ref : DAUBERT,TE & DANNER,RP (1985)

SMILES : c(ccc1)(c1)C
CHEM : Methyl-benzene or Toluene
MOL FOR: C7 H8
MOL WT : 92.14

SUMMARY MPBPWIN v1.40

Boiling Point: 125.72 deg C (Adapted Stein and Brown Method)

Melting Point: -78.09 deg C (Adapted Joback Method)
Melting Point: -40.26 deg C (Gold and Ogle Method)
Mean Melt Pt : -59.17 deg C (Joback; Gold,Ogle Methods)
Selected MP: -59.17 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):

(Using BP: 110.60 deg C (exp database))

(MP not used for liquids)

VP: 25.1 mm Hg (Antoine Method)
VP: 22.3 mm Hg (Modified Grain Method)
VP: 29.2 mm Hg (Mackay Method)

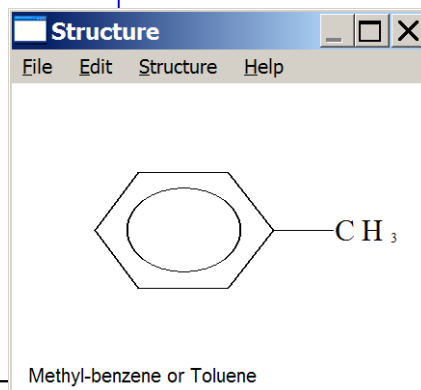
Selected VP: 23.7 mm Hg (Mean of Antoine & Grain methods)

TYPE	NUM	BOIL DESCRIPTION	COEFF	VALUE
Group	1	-CH3	21.98	21.98
Group	5	CH (aromatic)	28.53	142.65
Group	1	-C (aromatic)	30.76	30.76
*		Equation Constant		198.18

RESULT-uncorr	BOILING POINT in deg Kelvin	393.57
RESULT- corr	BOILING POINT in deg Kelvin	398.88
	BOILING POINT in deg C	125.72

TYPE	NUM	MELT DESCRIPTION	COEFF	VALUE
Group	1	-CH3	-5.10	-5.10
Group	5	CH (aromatic)	8.13	40.65
Group	1	-C (aromatic)	37.02	37.02
*		Equation Constant		122.50

RESULT	MELTING POINT in deg Kelvin	195.07
	MELTING POINT in deg C	-78.09



Melting point is calculated by two different methods, the mean value is determined, and the mean is selected as the melting point.

Vapor pressure is also calculated by different methods, and the mean value is selected as the vapor pressure.

WSKOWWIN™ to Estimate Water Solubility

What Does the WSKOWWIN™ Model Do?

WSKOWWIN™ estimates an octanol-water partition coefficient using the algorithms in the KOWWIN program and estimates a chemical's water solubility from this value. This method uses correction factors to modify the water solubility estimate based on regression against log Kow. This model can tell an assessor if the compound will dissolve in surface water. Water solubility is the degree to which a compound will dissolve in water. It is reported as the amount of the chemical (in milligrams) that will dissolve in 1 liter of water (mg/L).

How are the model predictions useful in risk assessment?

Knowing a chemical's water solubility (WS) is important because this can tell an assessor important information about the chemical's potential risk, for example:

- ❖ Chemicals with low WS:
 - Will have low concentration in aqueous media
 - Have a higher fish BCF
 - Are less likely to be absorbed into mammalian tissues.
- ❖ Chemicals with high WS:
 - Are more likely to be transported along with the water during storm events or to ground water; and
 - Have low log KOW values, and are more likely to be absorbed through GI tract, or lungs. The exception is the case of dispersible molecules like surfactants, and detergents, which can have high predicted log KOWs and can be absorbed through the lung.

Inputs: Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs:

- ❖ Molecular weight and formula
- ❖ Water solubility at 25°C (milligrams per liter)
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of Water Solubility Values

Solubility Classification (mg/L or ppm):

Very soluble	> 10,000
Soluble	> 1,000 - 10,000
Moderately sol.	> 100 - 1,000
Slightly soluble	> 0.1 - 100
Insoluble	< 0.1

Water Solubility Classifications

CAS No.	Chemical	Water Sol. (mg/L)
67561	Methanol	1.00E+06
67641	Acetone	2.20E+05
50000	Formaldehyde	5.74E+04
1912249	Atrazine	2.14E+02
60571	Dieldrin	1.46E-01

Important Notes

WSKOWWIN is not appropriate for dispersible compounds, including surfactants.

Where Can I Get WSKOWWIN™?

WSKOWWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitd1.htm. If you download and install EPI Suite™ you can run WSKOWWIN™ as a stand-alone model by putting a shortcut to the WSKOWNT.exe file on your Windows Desktop.

WSKOWWIN™ to Estimate Water Solubility

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

INPUTS: CAS Number 1912249 (atrazine)

RESULTS:

Water Sol: 214.1 mg/L

Experimental Water Solubility Database Match:

Name : ATRAZINE
CAS Num : 001912-24-9
Exp WSol : 34.7 mg/L (26 deg C)
Exp Ref : WARD, TM & WEBER, JB (1968)

SMILES : n(c(nc(n1)NC(C)C)NCC)c1CL

CHEM : Atrazine

MOL FOR: C8 H14 Cl1 N5

MOL WT : 215.69

----- WSKOW v1.40 Results -----

Log Kow (estimated) : 2.82

Log Kow (experimental): 2.61

Cas No: 001912-24-9

Name : Atrazine

Refer : Hansch, C et al. (1995)

Log Kow used by Water solubility estimates: 2.61

Equation Used to Make Water Sol estimate:

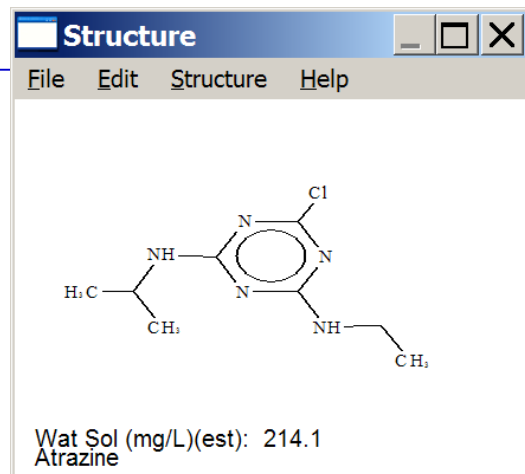
$\text{Log S (mol/L)} = 0.796 - 0.854 \log \text{Kow} - 0.00728 \text{ MW} + \text{Correction}$
(used when Melting Point NOT available)

Correction(s) : Value

No Applicable Correction Factors

Log Water Solubility (in moles/L) : -3.003

Water Solubility at 25 deg C (mg/L): 214.1



KOWWIN™ to Estimate Octanol-Water Partition Coefficient (KOW)

What Does the KOWWIN™ Model Do?

KOWWIN estimates the log octanol-water partition coefficient, log Kow, of chemicals using an atom/fragment contribution method.

How are the model predictions useful in risk assessment?

Knowing KOW will help the risk assessor know where the chemical will go in the stream. KOW indicates whether a chemical predominantly will be found in water (is hydrophilic) or in fatty tissue of animals or other organic materials (is lipophilic) in an aquatic environment. Lipophilic chemicals can bioaccumulate in fatty tissue of fish and bioconcentrate in animals (including humans) that consume the fish. Chemicals with a log KOW in the range of 4-7 may bioconcentrate significantly.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Log KOW
- ❖ Molecular weight and formula
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of KOW Values

	CAS Number	Chemical	log KOW
lipophilic	25051243	deca-PCB	10.2
	50293	DDT	6.8
	60571	Dieldrin	5.2
	1912249	Atrazine	2.6
	50000	Formaldehyde	0.4
hydrophilic	67641	Acetone	-0.2

log KOW of 0 indicates an equal affinity for lipids and for water

Important Notes

- ❖ KOW is often reported as a **log** due to the extremely wide range of measured KOW values.
- ❖ A log KOW of 0 indicates an equal affinity for lipids and for water.
- ❖ **There is a unique relationship between Log KOW and BCF:** As log KOW increases the solubility in lipids increases. This means an increase in the potential to bioconcentrate in organisms. This relationship begins to change around log KOW of 6. For chemicals with log KOW exceeding 6 the potential to bioconcentrate begins to drop approaching 0 at log KOW of 12.

Where Can I Get KOWWIN™?

KOWWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitel.htm. If you download and install EPI Suite™ you can run KOWWIN™ as a stand-alone model by putting a shortcut to the KOWWINNT.exe file on your Windows Desktop.

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

KOWWIN™ to Estimate Octanol-Water Partition Coefficient (KOW)

Sample Output from the KOWWIN™ Model

INPUTS: CAS Number 60571 (dieldrin)

RESULTS:

Log Kow (version 1.66 estimate): 5.45

Experimental Database Structure Match:

Name : Dieldrin
CAS Num : 000060-57-1
Exp Log P: 5.40
Exp Ref : DeBruijn,J et al. (1989)

Experimental Database Structure Match:

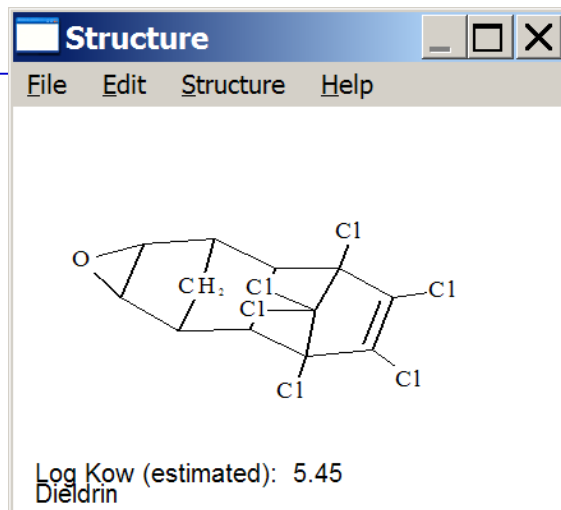
Name : Endrin
CAS Num : 000072-20-8
Exp Log P: 5.20
Exp Ref : DeBruijn,J et al. (1989)

SMILES : CLC4=C (CL) C5 (CL) C3C1CC (C2OC12) C3C4 (CL) C5 (CL) CL

CHEM : Dieldrin

MOL FOR: C12 H8 CL6 O1

MOL WT : 380.91



TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	-CH2- [aliphatic carbon]	0.4911	0.4911
Frag	6	-CH [aliphatic carbon]	0.3614	2.1684
Frag	1	C [aliphatic carbon - No H, not tert]	0.9723	0.9723
Frag	2	=CH- or =C< [olefinic carbon]	0.3836	0.7672
Frag	1	-O- [oxygen, aliphatic attach]	-1.2566	-1.2566
Frag	4	-CL [chlorine, aliphatic attach]	0.3102	1.2408
Frag	2	-CL [chlorine, olefinic attach]	0.4923	0.9846
Frag	2	-tert Carbon [3 or more carbon attach]	0.2676	0.5352
Factor	2	Fused aliphatic ring unit correction	-0.3421	-0.6842
Const		Equation Constant		0.2290
			Log Kow	= 5.4478

HENRYWIN™ to Estimate Henry's Law Constant

What Does the HENRYWIN™ Model Do?

HENRYWIN™ estimates the Henry's Law Constant (HLC) of an organic compound by two different methods. It also can estimate the HLC of an unknown compound based on the HLC of a known compound. The ratio of the vapor pressure to the water solubility is an estimate of the HLC that is sufficient for most purposes. HLC gives a relative measure of the volatility of a compound from water by measuring the extent to which a compound will partition between water and the air.

How are the model predictions useful in risk assessment?

Knowing the HLC helps the risk assessor predict the fate of the chemical once it is released to surface water. High HLC indicates chemical is likely to volatilize from solution and partition in air. Low HLC indicates chemical is not likely to volatilize and will remain in surface water.

Note: This estimate of the HLC does not apply for very water-soluble (i.e. miscible) compounds.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Henry's Law Constant estimated by bond contribution method and by group contribution method (best used for pesticides)
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of Henry's Law Constant Values

CAS Number	Chemical	HLC (atm-m ³ /mole)
75092	Dichloromethane	3.0E-03
50000	Formaldehyde	6.1E-05
67641	Acetone	4.0E-05
67561	Methanol	4.4E-06
60571	Dieldrin	5.4E-07

Volatility Classifications

Very volatile	$\geq 10^{-1}$
Volatile	$10^{-1} - 10^{-3}$
Moderately volatile	$10^{-3} - 10^{-5}$
Slightly volatile	$10^{-5} - 10^{-7}$
Nonvolatile	$< 10^{-7}$

Where Can I Get HENRYWIN™?

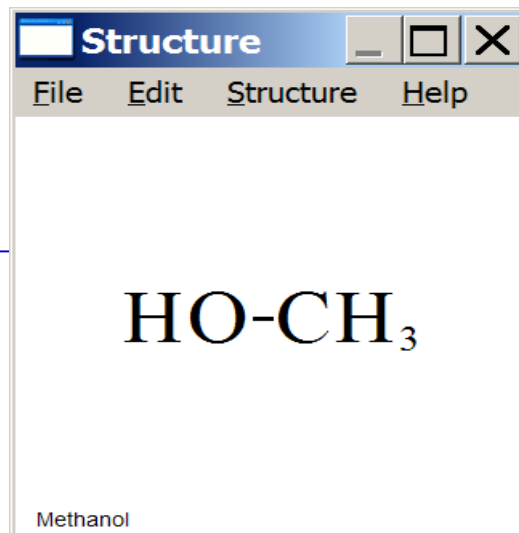
HENRYWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedi.htm. If you download and install EPI Suite™ you can run HENRYWIN™ as a stand-alone model by putting a shortcut to the HENRYNT.exe file on your Windows Desktop.

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

HENRYWIN™ to Estimate Henry's Law Constant

Sample Output From the HENRYWIN™ Model



INPUTS: CAS Number 67561 (methanol)

RESULTS:

Bond Est : 4.27E-006 atm-m3/mole

Group Est: 3.62E-006 atm-m3/mole

SMILES : OC

CHEM : Methanol

MOL FOR: C1 H4 O1

MOL WT : 32.04

----- HENRYWIN v3.10 Results -----

Experimental Database Structure Match:

Name : METHANOL
 CAS Num : 000067-56-1
 Exp HLC : 4.55E-06 atm-m3/mole
 Temper : 25 deg C
 Exp Ref : GAFFNEY,JS ET AL. (1987)

Two methods are used to estimate HLC. The group contribution method is best used for pesticides.

CLASS	BOND CONTRIBUTION DESCRIPTION	COMMENT	VALUE
HYDROGEN	3 Hydrogen to Carbon (aliphatic) Bonds		-0.3590
HYDROGEN	1 Hydrogen to Oxygen Bonds		3.2318
FRAGMENT	1 C-O		1.0855
FACTOR	* Non-cyclic alkyl or olefinic alcohol		-.2000
RESULT	BOND ESTIMATION METHOD for LWAPC VALUE	TOTAL	3.758

HENRYs LAW CONSTANT at 25 deg C = 4.27E-006 atm-m3/mole
 = 1.74E-004 unitless

	GROUP CONTRIBUTION DESCRIPTION	COMMENT	VALUE
	1 CH3 (X)		-0.62
	1 O-H (C)		4.45
RESULT	GROUP ESTIMATION METHOD for LOG GAMMA VALUE	TOTAL	3.83

HENRYs LAW CONSTANT at 25 deg C = 3.62E-006 atm-m3/mole
 = 1.48E-004 unitless

PCKOCWIN™ to Estimate Organic Carbon Adsorption Coefficient (KOC)

What Does the PCKOCWIN™ Model Do?

PCKOCWIN™ predicts a chemical's soil adsorption coefficient (KOC), which is the ability of a chemical to sorb to the organic portion of soil and sediment. KOC estimations are based on the Sabljic molecular connectivity method with improved correction factors. KOC is the ratio of amount of chemical adsorbed per unit mass of organic carbon (the "OC") in soils, sediments, or sludge to the concentration of the chemical in the solution at equilibrium. KOC indicates whether a chemical is likely to be found in water or the organic carbon portion of soils or sediments.

How are the model predictions useful in risk assessment?

KOC provides an indication of partitioning to sediments and sludge. Low KOC values suggest the chemical is likely to remain in water, and possibly migrate with ground water, because it is not likely to sorb to soils, sediments, or sludge. High KOC value suggests the chemical will sorb to soils and sediments, or sludge, and is not likely to be found in surface water or migrate with ground water.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Estimated KOC
- ❖ Molecular weight and formula
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of KOC Values

CAS Number	Chemical	Log KOC
60571	Dieldrin	4.025
1912249	Atrazine	2.362
75092	Dichloromethane	1.376
106898	Epichlorohydrin	0.652
67641	Acetone	0.297

KOC Classifications

Very strong	≥ 4.5
Strong	3.5 - 4.4
Moderate	2.5 - 3.4
Low	1.5 - 2.4
Negligible	< 1.5

Important Notes

- ❖ Like KOW, KOC is also often reported as a log due to the extremely wide range of measured KOC values.
- ❖ When $\text{Log KOC} \geq 4.5$ chemical will largely be removed by sorption to sludge in wastewater treatment plants.

Where Can I Get PCKOCWIN™?

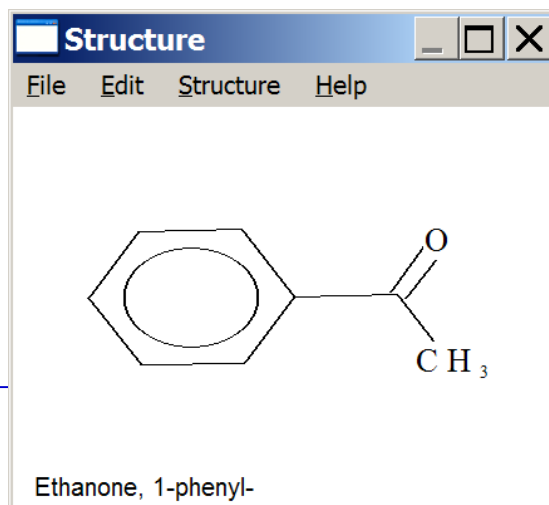
PCKOCWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedl.htm. If you download and install EPI Suite™ you can run PCKOCWIN™ as a stand-alone model by putting a shortcut to the PCKOCNT.exe file on your Windows Desktop.

PCKOCWIN™ to Estimate Organic Carbon Adsorption Coefficient (KOC)

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

Sample Output From the PCKOCWIN™ Model



INPUTS: CAS Number 98-86-2
(Acetophenone)

RESULTS:

Koc (estimated): 46.2

SMILES : O=C(c(cccc1) c1) C
CHEM : Ethanone, 1-phenyl-
MOL FOR: C8 H8 O1
MOL WT : 120.15

----- PCKOCWIN v1.66 Results -----

First Order Molecular Connectivity Index :	4.305
Non-Corrected Log Koc :	2.9123
Fragment Correction(s):		
1 Ketone (-C-CO-C-) :	-1.2477
Corrected Log Koc :	1.6646

Estimated Koc: 46.2

Models to Estimate Chemical Fate in the Environment

The ENVIRONMENTAL FATE MODELS included in this section are:

- ❖ AOPWIN™
- ❖ HYDROWIN™
- ❖ BIOWIN™
- ❖ BCFWIN™
- ❖ STPWIN™
- ❖ LEV3EPI™

Following are brief fact sheets providing information on the models OPPT has developed and uses to estimate environmental fate of chemicals. Information provided on each model includes:

- ❖ What fate property does the model estimate?
- ❖ What is significant about the fate property to risk assessment?
- ❖ Why is knowing fate properties important?
- ❖ Why would I want to use the model?
- ❖ What do I need to run the model?
- ❖ What are the inputs and outputs for the model?

AOPWIN™ to Estimate Atmospheric Oxidation Potential

What Does the AOPWIN™ Model Do?

AOPWIN™ estimates rate constants and half-lives of atmospheric reactions of organic compounds released to the air with hydroxyl radicals (-OH) and with ozone in the atmosphere. estimates the rate at which certain organic compounds will be destroyed by reactions with compounds in the atmosphere.

How are the model predictions useful in risk assessment?

The rate at which an organic compound will be oxidized (destroyed) is an indication of the length of time the compound may reside in the atmosphere.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file
- ❖ Hydroxyl radical (-OH) rate constant and half-life
- ❖ Ozone reaction constant and half-life (for olefins and acetylenes only)

Examples of Atmospheric Oxidation Potential Values

CAS Number	Chemical	AOP 1/2 Life (days)
75092	Dichloromethane	79.3
67641	Acetone	52.4
67561	Methanol	17.4
60571	Dieldrin	1.2
1912249	Atrazine	0.4

Atmospheric Oxidation Potential Classifications

Rapid	≤ 2 hrs
Moderate	2 hrs - ≤ 1 day
Slow	> 1 day - ≤ 10 days
Negligible	> 10 days

Important Notes

- ❖ Half-life of >2 days indicates the chemical may be persistent in air.
- ❖ If a chemical has a high AOP rate there still is a potential for inhalation exposure if the travel time from source to receptor is greater than the time for complete oxidation of the compound.

Where Can I Get AOPWIN™?

AOPWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedl.htm. If you download and install EPI Suite™ you can run AOPWIN™ as a stand-alone model by putting a shortcut to the AOPWINNT.exe file on your Windows Desktop.

AOPWIN™ to Estimate Atmospheric Oxidation Potential

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

Sample Output from the AOPWIN™ Model

INPUTS: CAS Number 1912249 (atrazine)

RESULTS:

SMILES : n(c(nc(n1)NC(C)C)NCC)c1Cl
 CHEM : Atrazine
 MOL FOR : C8 H14 Cl1 N5
 MOL WT : 215.69

-----SUMMARY : HYDROXYL RADICALS-----

Hydrogen Abstraction	= 24.2300 E-12 cm ³ /molecule-sec
Reaction with N, S, and -OH	= 0.0000 E-12 cm ³ /molecule-sec
Addition to Triple Bonds	= 0.0000 E-12 cm ³ /molecule-sec
Addition to Olefinic Bonds	= 0.0000 E-12 cm ³ /molecule-sec
**Addition to Aromatic Rings	= 0.1176 E-12 cm ³ /molecule-sec
Addition to Fused Rings	= 0.0000 E-12 cm ³ /molecule-sec

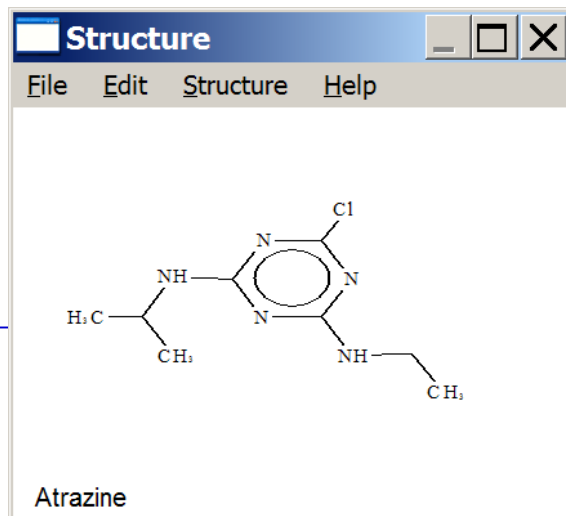
OVERALL OH	=	27.3476 E-12 cm ³ /molecule-sec
HALF-LIFE	=	0.391 Days (12-hr day; 1.5E6 OH/cm ³)
HALF-LIFE	=	4.693 Hrs

. . . . * * Designates Estimation(s) Using ASSUMED Value(s)

-----SUMMARY (AOP v1.90): OZONE REACTION-----

* * * * NO OZONE REACTION ESTIMATION * * * *
 (ONLY Olefins and Acetylenes are Estimated)

Experimental Database : NO Structure Matches



Reactions with ozone are estimated only for olefins and acetylenes.

HYDROWIN™ to Estimate Hydrolysis

What Does the HYDROWIN™ Model Do?

HYDROWIN™ estimates acid- and base-catalyzed rate constants for chemicals in certain classes (esters, carbamates, epoxides, halomethanes, and certain alkyl halides). A chemical's hydrolytic half-life under typical environmental conditions is also determined. Neutral hydrolysis rates are currently not estimated.

How are the model predictions useful in risk assessment?

Understanding a chemical's rates of hydrolysis (the breakdown of a chemical by its reaction with water) will help the risk assessor estimate the concentration of the compound in treatment systems and after it is released to surface water, and how long the chemical and/or its hydrolysis products will remain in water bodies after release. The chemical can be catalyzed (broken down) by acids (hydronium) or bases (hydroxide ions).

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Estimated hydrolysis at 25°C
- ❖ Half-life at pHs 8 and 7
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Examples of Hydrolysis Values

CAS Number	Chemical	Hydrolysis 1/2 Life (yrs)
51796	Carbamic acid, ethyl ester	3326.534
110383	Ethyl decanolate	7.7

Where Can I Get HYDROWIN™?

HYDROWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedi.htm. If you download and install EPI Suite™ you can run HYDROWIN™ as a stand-alone model by putting a shortcut to the HYDRONT.exe file on your Windows Desktop.

Saving Output

Results can be printed when displayed. After results are displayed click on "Save Results" and you can save results as a ".dat" file that can be opened using MSWord or WordPerfect. Output can also be copied (click on "Copy") through the Windows Clipboard. Structures can be saved as an ISIS ".skc" file or through the Windows Clipboard. Further explanations are given in "Help" on the Results page.

BIOWIN™ to Estimate Biodegradation

What Does the BIOWIN™ Model Do?

BIOWIN provides estimates of biodegradability useful in chemical screening, including the likelihood of passing a ready biodegradability test plus the approximate time required for a compound to biodegrade in a stream. Biodegradation is the destruction of a compound by biota, typically microorganisms, in the environment. Primary biodegradation is a change in molecular structure, and ultimate biodegradation is the complete conversion of the molecule to CO₂ and H₂O.

BIOWIN has 6 models. The linear and a non-linear regression models, called BIOWIN 1 and BIOWIN 2, are based on regressions against 36 preselected chemical substructures plus molecular weight of experimental biodegradation data for 295 chemicals. The models correctly classified 90% of the chemicals in their training set as rapidly or not rapidly *biodegradable*. BIOWIN 3 and BIOWIN 4 estimate the approximate time required for ultimate and primary biodegradation, respectively, of an organic compound in streams. They are based on regressions of biodegradability estimates from a survey of experts for a suite of 200 organic chemicals, against the same chemical substructures plus molecular weight. BIOWIN 5 and BIOWIN 6 estimate the probability of passing the OECD 301C ready biodegradability test (MITI-1 test). They are based on linear (BIOWIN 5) and nonlinear (BIOWIN 6) regressions of data from the Japanese MITI database against a modified set of chemical substructures plus molecular weight. Results were slightly better for the nonlinear model.

The EPI Suite of models were developed by Syracuse Research Corporation. All six of the models were developed under contract to the U.S EPA, OPPT, in support of Section 5 of TSCA.

How are the model predictions useful in risk assessment?

Whether a substance is readily biodegradable (RB) or not readily biodegradable (NRB) may have significant economic and regulatory impact. For example, in the European Community (EC) it is an important factor in classification and labeling under the dangerous substances directive. In the US, it is one of a small number of environmental fate data requirements included in the voluntary High Production Volume Chemical (HPVC) Challenge program. Applications in design and formulation of safer chemical products ("green chemistry") are also numerous because ready biodegradability is a useful basis for comparing alternatives. Recent work has demonstrated that model "batteries" consisting of BIOWIN3 and either BIOWIN5 or BIOWIN6 can be quite successful in classifying compounds as readily or not readily biodegradable; i.e. false positives for ready biodegradability are significantly reduced in number as compared to any individual model.

Knowing the time approximate required for a chemical to be broken down will help the risk assessor estimate the likely concentration of the chemical at various downstream locations and times after release to surface water. BIOWIN3 provides this information, which can be used in a variety of ways including serving as the basis for half-lives needed for running other models such as the PBT Profiler.

Chemicals with very long biodegradation times may be highly persistent in the environment IF they are not subject to destruction by other processes such as photolysis, hydrolysis, etc.

Formal pass criteria for OECD ready biodegradability tests:

>60 % of theoretical CO₂ evolution or biochemical oxygen demand in 28 days (>50% is also likely to be evidence of complete degradation of a compound, though this value is not formally recognized by the OECD)

>70% loss of dissolved organic carbon (DOC) derived from test compound.

General guidance for characterizing biodegradation rates:

Rapid	≥ 60% in	≤ 7 days
Moderate	≥ 30% in	≤ 28 days
Slow	< 30% in	≤ 28 days
Very slow	< 30% in	> 28 days

Examples of Biodegradation Values

<u>CAS Number</u>	<u>Chemical</u>	<u>Ultimate Biodeg.</u>
60571	Dieldrin	recalcitrant
1912249	Atrazine	months
75092	Dichloromethane	weeks-months
67641	Acetone	weeks
67561	Methanol	days-weeks

Inputs

CAS Registry Number or chemical structure in SMILES notation. When running models in the EPI Suite, available measured data should be entered because this will give more reliable estimates. This program can be operated in a “Batch Mode” so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Predicted primary and ultimate biodegradation in hours, days, weeks, or months; also predicted, via separate but linked models, the probability of rapid biodegradation using two different methods; also predicted, via separate but linked models, the probability of passing a MITI-I (OECD 301C) ready biodegradability test
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Where Can I Get BOWIN™?

BOWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedi.htm. If you download and install EPI Suite™ you can run BOWIN™ as a stand-alone model by putting a shortcut to the BOWINNT.exe file on your Windows Desktop.

Saving Output

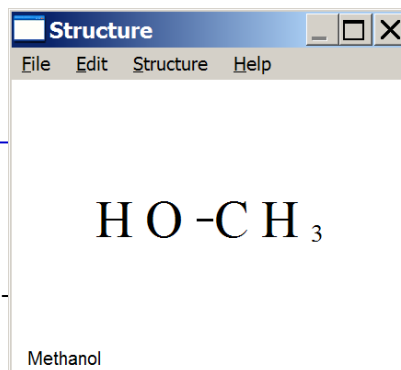
Results can be printed when displayed. After results are displayed click on “Save Results” and you can save results as a “.dat” file that can be opened using MSWord or WordPerfect. Output can also be copied (click on “Copy”) through the Windows Clipboard. Structures can be saved as an ISIS “.skc” file or through the Windows Clipboard. Further explanations are given in “Help” on the Results page.

Important Notes

- Remember that BOWIN can be run using SMILES notations instead of CAS numbers.
- If your chemical is not in the SMILECAS database, you will need to write the SMILES and run the model using SMILES.
- BOWIN can be run as a part of the EPI Suite.
- Biodegradation Probability > 0.5 from BOWIN1 or 2 indicates “rapid biodegradation”; for BOWIN5 or 6, indicates | Readily Degradable.
- Biodegradation Probability < 0.5 from BOWIN1 or 2 indicates “not rapid biodegradation”; for BOWIN5 or 6, indicates | NOT Readily Degradable.
- Biodegradation of “weeks” or faster from BOWIN3 in combination with biodegradation probability > 0.5 from BOWIN5 (or BOWIN6) is even more reliable in indicating | Readily Degradable
- When running models in the EPI Suite, available measured data should be entered because this will give more reliable estimates.

BIOWIN™ to Estimate Biodegradation

Sample Output from the BIOWIN™ Model



INPUTS: CAS Number = 67561 (methanol)

RESULTS:

SMILES : OC
CHEM : Methanol
MOL FOR : C1 H4 O1
MOL WT : 32.04

----- BIOWIN v4.00 Results -----

Linear Model Prediction : Biodegrades Fast
Non-Linear Model Prediction: Biodegrades Fast
Ultimate Biodegradation Timeframe: Days-Weeks
Primary Biodegradation Timeframe: Days
MITI Linear Model Prediction : Readily Degradable
MITI Non-Linear Model Prediction: Readily Degradable

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	0.1587	0.1587
MolWt	*	Molecular Weight Parameter		-0.0153
Const	*	Equation Constant		0.7475

RESULT LINEAR BIODEGRADATION PROBABILITY 0.8910

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	1.1178	1.1178
MolWt	*	Molecular Weight Parameter		-0.4550

RESULT NON-LINEAR BIODEGRADATION PROBABILITY 0.9752

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast
A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	0.1600	0.1600
MolWt	*	Molecular Weight Parameter		-0.0708
Const	*	Equation Constant		3.1992

RESULT SURVEY MODEL - ULTIMATE BIODEGRADATION 3.2883

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	0.1294	0.1294
MolWt	*	Molecular Weight Parameter		-0.0462
Const	*	Equation Constant		3.8477

RESULT SURVEY MODEL - PRIMARY BIODEGRADATION 3.9310

Result Classification: 5.00 -> hours 4.00 -> days 3.00 -> weeks
(Primary & Ultimate) 2.00 -> months 1.00 -> longer

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	0.1611	0.1611
Frag	1	Methyl [-CH3]	0.0004	0.0004
MolWt	*	Molecular Weight Parameter		-0.0953
Const	*	Equation Constant		0.7121

RESULT MITI LINEAR BIODEGRADATION PROBABILITY 0.7784

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	Aliphatic alcohol [-OH]	1.0041	1.0041
Frag	1	Methyl [-CH3]	0.0194	0.0194
MolWt	*	Molecular Weight Parameter		-0.9250

RESULT MITI NON-LINEAR BIODEGRADATION PROBABILITY 0.9324

A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable
A Probability Less Than 0.5 indicates --> NOT Readily Degradable

This chemical is predicted to biodegrade completely in days to weeks.

The 6 Models in BIOWIN are:

BIOWIN 1

BIOWIN 2

BIOWIN 3

BIOWIN 4

BIOWIN 5

BIOWIN 6

BCFWIN™ to Estimate Bioconcentration Factor

What Does the BCFWIN™ Model Do?

BCFWIN™ calculates the **BioConcentration Factor** and its logarithm from the log KOW. The methodology is analogous to that for WSKOWWIN. Both are based on log Kow and correction factors. A bioconcentration factor (BCF) is the ratio (in L/kg) of a chemical's concentration in the tissue of an aquatic organism to its concentration in the ambient water, when exposure of the organism is to waterborne chemicals only (i.e., not to chemical in the organism's diet or sorbed to ingested particles).

The EPI Suite of models were developed by Syracuse Research Corporation. The BCFWIN Model was developed under contract to the U.S. EPA, OPPT, in support of Section 5 of TSCA.

How are the model predictions useful in risk assessment?

Knowing the fish BCF helps the risk assessor predict the potential for a chemicals to bioaccumulate in lipids (fatty tissue) of aquatic organisms.

Bioconcentration Potential

High	≥ 5,000
Moderate	1,000 – 5,000
Low	< 1,000

Relationship Between log KOW and Fish BCF

As log KOW increases the solubility in lipids increases. This generally means an increase in the potential to bioconcentrate in aquatic organisms. This relationship begins to change around log KOW of 6. Above this value the situation is more complex because low water solubility limits the rate of uptake by the exposed organism. This means equilibrium may take a very long time to be achieved in bioconcentration studies, possibly too long to be practical. A result is that published data on BCF seem to show that BCF drops with increasing log KOW above log KOW of about 6. Some experts say that "true" bioconcentration potential continues to increase above log KOW ca. 6. Most likely, dietary exposure becomes dominant and exposure to waterborne chemical insignificant (remember—waterborne chemical only is a basic assumption for BCF to be valid!). What this really means is that **no simple "BCF/log KOW" relationship applies** at higher values of log KOW. That is, estimated BCF from BCFWIN is best used only below log KOW ca. 6.

Inputs

CAS Registry Number or chemical structure in SMILES notation. When running models in the EPI Suite, available measured data should be entered because this will give more reliable estimates. This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Molecular weight and formula
- ❖ Estimated Log BCF
- ❖ Estimated log KOW

Examples of Bioconcentration Factor Values

CAS Number	Chemical	Log BCF
8001352	Toxaphene	4.5
12789036	Chlordane	4.8
60571	Dieldrin	3.7
108703	1,3,5-Trichlorobenzene	2.7

Where Can I Get BCFWIN™?

BCFWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/EPI_SuiteI.htm. If you download and install EPI Suite™ you can run BCFWIN™ as a stand-alone model by putting a shortcut to the BCFWINNT.exe file on your Windows Desktop.

Saving Output

Results can be printed when displayed. After results are displayed click on “Save Results” and you can save results as a “.dat” file that can be opened using MSWord or WordPerfect. Output can also be copied (click on “Copy”) through the Windows Clipboard. Structures can be saved as an ISIS “.skc” file or through the Windows Clipboard. Further explanations are given in “Help” on the Results page.

Sample Output From the BCFWIN™ Model

INPUTS: CAS Number 8001352
(toxaphene)

RESULTS:

Log BCF (v2.14 estimate): 3.75

SMILES : CLC(C(CL)C1C2)C(C2(CL)CL)(C1(C(CL)CL)CCL)CCL

CHEM : Toxaphene

MOL FOR: C10 H10 CL8

MOL WT : 413.82

----- Bcfwin v2.14 -----

Log Kow (estimated) : 6.79

Log Kow (experimental): 5.78

Log Kow used by BCF estimates: 5.78

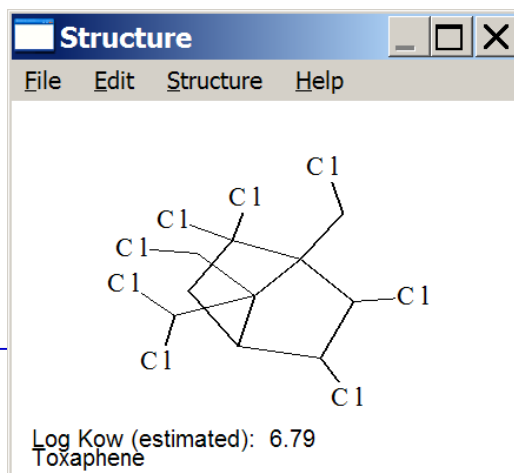
Equation Used to Make BCF estimate:

$\text{Log BCF} = 0.77 \log \text{Kow} - 0.70 + \text{Correction}$

Correction(s):	Value
----------------	-------

No Applicable Correction Factors

Estimated Log BCF = 3.751 (BCF = 5631)



STPWIN™ to Estimate Percent Removal in Wastewater Treatment

What Does the STPWIN™ Model Do?

STPWIN™ predicts the percent of a compound that will be removed from the waste water in wastewater treatment. Values are given for the total removal and three contributing processes (biodegradation, sorption to sludge, and stripping to air) for a standard system and set of operating conditions. STP is “Sewage Treatment Plant” and POTW is “Publicly Owned Treatment Works”. Both are names for utilities that treat waste water and usually discharge the treated water to nearby surface water bodies.

How are the model predictions useful in a risk assessment?

Knowing how much of the chemical will be removed from the waste water during wastewater treatment enables the risk assessor to predict how much of the chemical may be discharged by the POTW to surface water and potentially affect aquatic life. How much chemical is discharged to surface water may also affect subsequent uptake by humans via drinking water that is derived from surface water.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a “Batch Mode” so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs

- ❖ Estimated percent removal in wastewater treatment
- ❖ Overall chemical mass balance

Examples of Removal Rate Values

CAS Number	Chemical	Percent Removal
60571	Dieldrin	83.11
75092	Dichloromethane	56.91
50000	Formaldehyde	67.3
67641	Acetone	73.06
108952	Phenol	97.47

Where Can I Get STPWIN™?

STPWIN™ has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedl.htm.

Saving Output

Results can be printed when displayed. After results are displayed click on “Save Results” and you can save results as a “.dat” file that can be opened using MSWord or WordPerfect. Output can also be copied (click on “Copy”) through the Windows Clipboard. Structures can be saved as an ISIS “.skc” file or through the Windows Clipboard. Further explanations are given in “Help” on the Results page.

STPWIN™ to Estimate Percent Removal in Wastewater Treatment

Sample Output From the STPWIN™ Model

INPUTS: SMILES : c1ccccc1

RESULTS:

SMILES : c1ccccc1

CHEM : Chemical B

MOL FOR: C6 H6

MOL WT : 78.11

Physical Property Inputs:

Water Solubility (mg/L): 1800

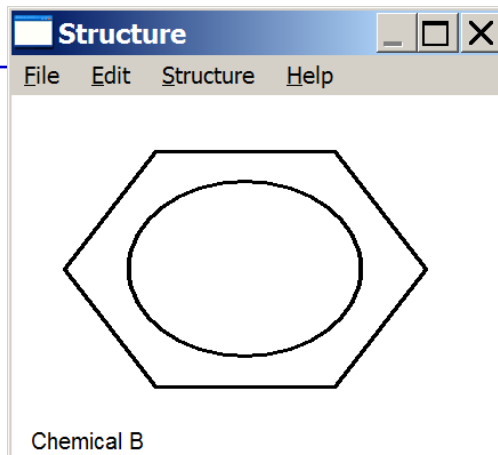
Vapor Pressure (mm Hg) : 95.3

Henry LC (atm-m3/mole) : -----

Log Kow (octanol-water) : -----

Boiling Point (deg C) : -----

Melting Point (deg C) : -----



STP Fugacity Model: Predicted Fate in a Wastewater Treatment Facility

PROPERTIES OF: Chemical B

Molecular weight (g/mol) 78.11

Aqueous solubility (mg/l) 1800

Vapour pressure (Pa) 12705.6

(atm) 0.125395

(mm Hg) 95.3

Henry 's law constant (Atm-m3/mol) 0.00555

Air-water partition coefficient 0.226978

Octanol-water partition coefficient (Kow) 134.896

Log Kow 2.13

Biomass to water partition coefficient 27.7793

Temperature [deg C] 25

Biodeg rate constants (h⁻¹), half life in biomass (h) and in 2000 mg/L MLSS (h):

-Primary tank	0.00	526.34	10000.00
-Aeration tank	0.00	526.34	10000.00
-Settling tank	0.00	526.34	10000.00

Predicted
Removal Rate in
Waste Water
Treatment is
69%

STP Overall Chemical Mass Balance:

	g/h	mol/h	percent
Influent	1.00E+001	1.3E-001	100.00
Primary sludge	5.63E-002	7.2E-004	0.56
Waste sludge	5.46E-002	7.0E-004	0.55
Primary volatilization	1.25E-001	1.6E-003	1.25
Settling volatilization	1.10E-001	1.4E-003	1.10
Aeration off gas	6.54E+000	8.4E-002	65.43
Primary biodegradation	1.82E-003	2.3E-005	0.02
Settling biodegradation	1.76E-004	2.2E-006	0.00
Aeration biodegradation	2.35E-003	3.0E-005	0.02
Final water effluent	3.11E+000	4.0E-002	31.06
Total removal	6.89E+000	8.8E-002	68.94
Total biodegradation	4.35E-003	5.6E-005	0.04

LEV3EPI™ Model to Estimate Fugacity

What Does the LEV3EPI™ Model Do?

The LEV3EPI Fugacity model is based on the LEVEL III fugacity model, developed by Don Mackay of Canadian Environmental Modelling Centre, Trent University, Ontario, Canada. LEV3EPI is a non-equilibrium, steady-state multimedia fate model that provides screening level predictions of environmental partitioning (percent in each media) of chemicals between air, soil, sediment, and water under steady state conditions for a default model "environment"; various defaults can be changed by the user. A risk assessor can use this model to estimate where a chemical is most likely to reside once it has been released to the environment.

How are the model predictions useful in risk assessment?

If the risk assessor understands a chemical's potential environmental partitioning he/she can use this information to manage the release scenario to minimize detrimental impacts to human health and the environment.

Inputs

Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measured physical/chemical properties and environmental half-lives should be entered (If not available these properties will be estimated by EPISuite™ components.)

Outputs

- ❖ partition coefficients
- ❖ Z values
- ❖ fugacity of each medium
- ❖ intermedia transport rates and D values
- ❖ reaction and advection D values and loss rates
- ❖ residence times or persistences (overall, reaction, and advection)
- ❖ concentrations and amounts for each medium
- ❖ summary diagram
- ❖ charts of key results, "readme.txt" file with more detailed technical information in a zipped file.

Examples of Fugacity Values

CAS RN	Chemical	Persistence (hrs)
8001352	Toxaphene	4260
12789036	Chlordane	4730
60571	Dieldrin	3040
108703	1,3,5-Trichlorobenzene	791
108952	Phenol	290

Important Notes

Default emission rates are equal amounts (1,000 kg/hr) to air, soil, and water (direct discharges to sediment are unlikely). The model treats a generic environment of 100,000 square km with 10% water; 90% soil surface; water depth 20 m; soil depth 20 cm; sediment depth 5 cm; atmospheric height 1000 m. The LEV3EPI™ model provides a representative environment about the size of the state of Ohio. It is important to note, however, that the percent in each medium will change as a function of the size of the compartments chosen. Moreover, the results of this model are calculated at steady state; a condition that may not occur in the environment (on a global scale).

LEV3EPI™ Model to Estimate Fugacity

Where Can I Get the LEV3EPI™ Model?

The LEV3EPI Fugacity model has been incorporated into the EPI Suite™ which is available at www.epa.gov/opptintr/exposure/docs/episuitedl.htm. If you download and install EPI Suite™ you can run LEV3EPI™ as a stand-alone model by putting a shortcut to the LEV3NT.exe file on your Windows Desktop.

Saving Output

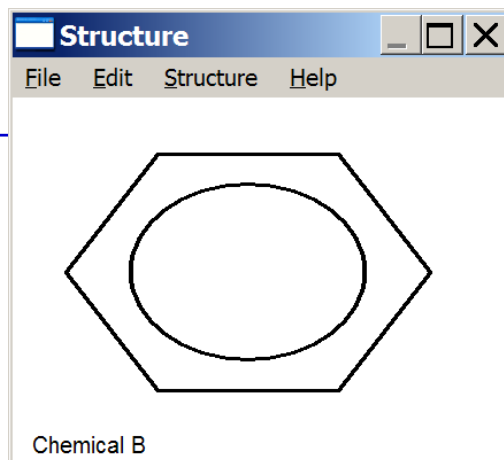
Results can be printed when displayed. After results are displayed click on “Save Results” and you can save results as a “.dat” file that can be opened using MSWord or WordPerfect. Output can also be copied (click on “Copy”) through the Windows Clipboard. Structures can be saved as an ISIS “.skc” file or through the Windows Clipboard. Further explanations are given in “Help” on the Results page.

Sample Output From the LEV3EPI™ Model

Run with default emission rates which assumes equal rates to Air, Water, Soil. Sediment is part of the water column.

Benzene (SMILES c1ccccc1)

	Percent in each media	Half-Life (hrs)
Air	38.0	209
Water	48.0	900
Soil	14.0	900
Sediment	0.2	0



Level III Fugacity Model (Full-Output):

```

=====
Chem Name      : Chemical B
Molecular Wt   : 78.11
Henry's LC     : 0.00555 atm-m3/mole (Henry database)
Vapor Press    : 87.2 mm Hg (MPBPVP™ program)
Log Kow        : 2.13 (Kowwin program)
Soil Koc       : 55.3 (calc by model)
  
```

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	37.6	209	1000
Water	48.4	900	1000
Soil	13.8	900	1000
Sediment	0.202	3.6e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	5.91e-010	627	1.89e+003	20.9	62.9
Water	8.65e-008	188	244	6.25	8.12
Soil	1.64e-007	53.4	0	1.78	0
Sediment	7.75e-008	0.196	0.0203	0.00652	0.000677

```

Persistence Time: 168 hr
Reaction Time:    579 hr
Advection Time:   236 hr
Percent Reacted:  28.9
Percent Advected: 71.1
  
```

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):

```

Air:      208.7
Water:    900
Soil:     900
Sediment: 3600
Biowin estimate: 2.441 (weeks-months)
  
```

Advection Times (hr):

```

Air:      100
Water:    1000
Sediment: 5e+004
  
```


Models to Estimate Hazard to Humans and the Environment

The HAZARD MODELS included in this section are:

- ❖ OncoLogic
- ❖ ECOSAR
- ❖ Screening for Non-Cancer Human Health Effects (not a computerized model, but a step-wise screening protocol)
- ❖ PBT Profiler

Following are brief fact sheets providing information on the models OPPT has developed and uses to estimate environmental fate of chemicals. Information provided on each model includes:

- ❖ What hazard endpoint does the model estimate?
- ❖ What is significant about the hazard endpoint to risk assessment?
- ❖ Why is knowing hazard properties important?
- ❖ Why would I want to use the model?
- ❖ What do I need to run the model?
- ❖ What are the inputs and outputs for the model?

OncoLogic to Estimate Potential Carcinogenicity

What Does the OncoLogic Model Do?

OncoLogic estimates the potential for a chemical to cause cancer in humans using the known carcinogenicity of chemicals with similar chemical structures, information on mechanisms of action, short-term predictive tests, epidemiological studies, and expert judgment. OncoLogic can tell the risk assessor the potential for the chemical to cause cancer in humans (carcinogenicity) and help the assessor determine if further testing of the chemical (bioassays) may be advisable.

How are the model predictions useful in risk assessment?

An understanding of the potential for the chemical to cause cancer helps the risk assessor estimate the impact of the release of that chemical on the surrounding human population.

Inputs

- ❖ Class of chemical (fiber, polymer, metal, or organic compound)
- ❖ Chemical structure
- ❖ Functional groups present
- ❖ Additional properties listed in Flow Diagrams for each module.

Outputs

- ❖ Summary of predicted concern level (high to low)
- ❖ Line of reasoning for estimation

Important Notes

OncoLogic users need: Good understanding of organic chemistry; Chemical class of the compound; Certain physical and chemical properties of the compound

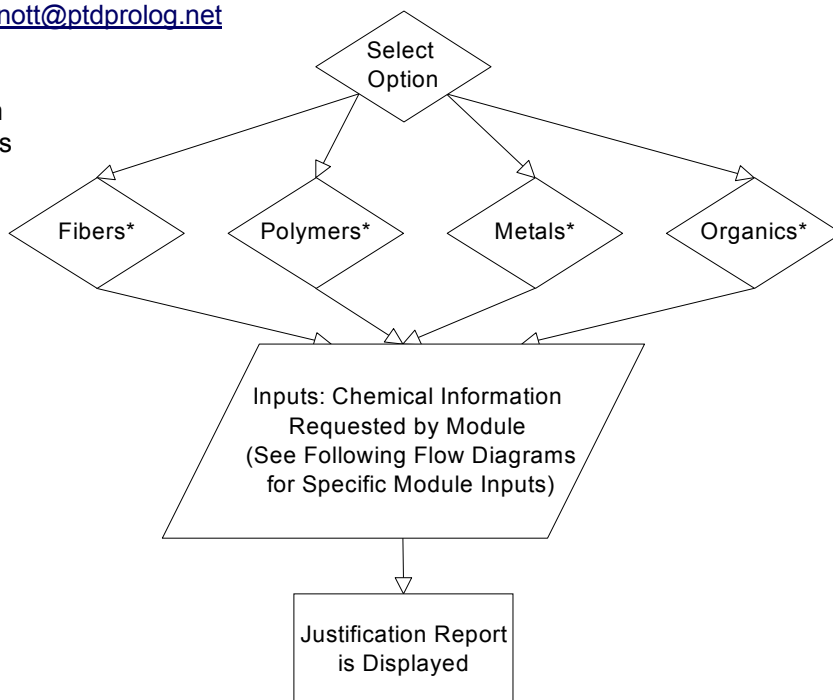
OncoLogic has modules to estimate carcinogenicity of 4 types of compounds: (1) Fibers, (2) Metals, (3) Polymers, and (4) Organics

Where Can I Get OncoLogic?

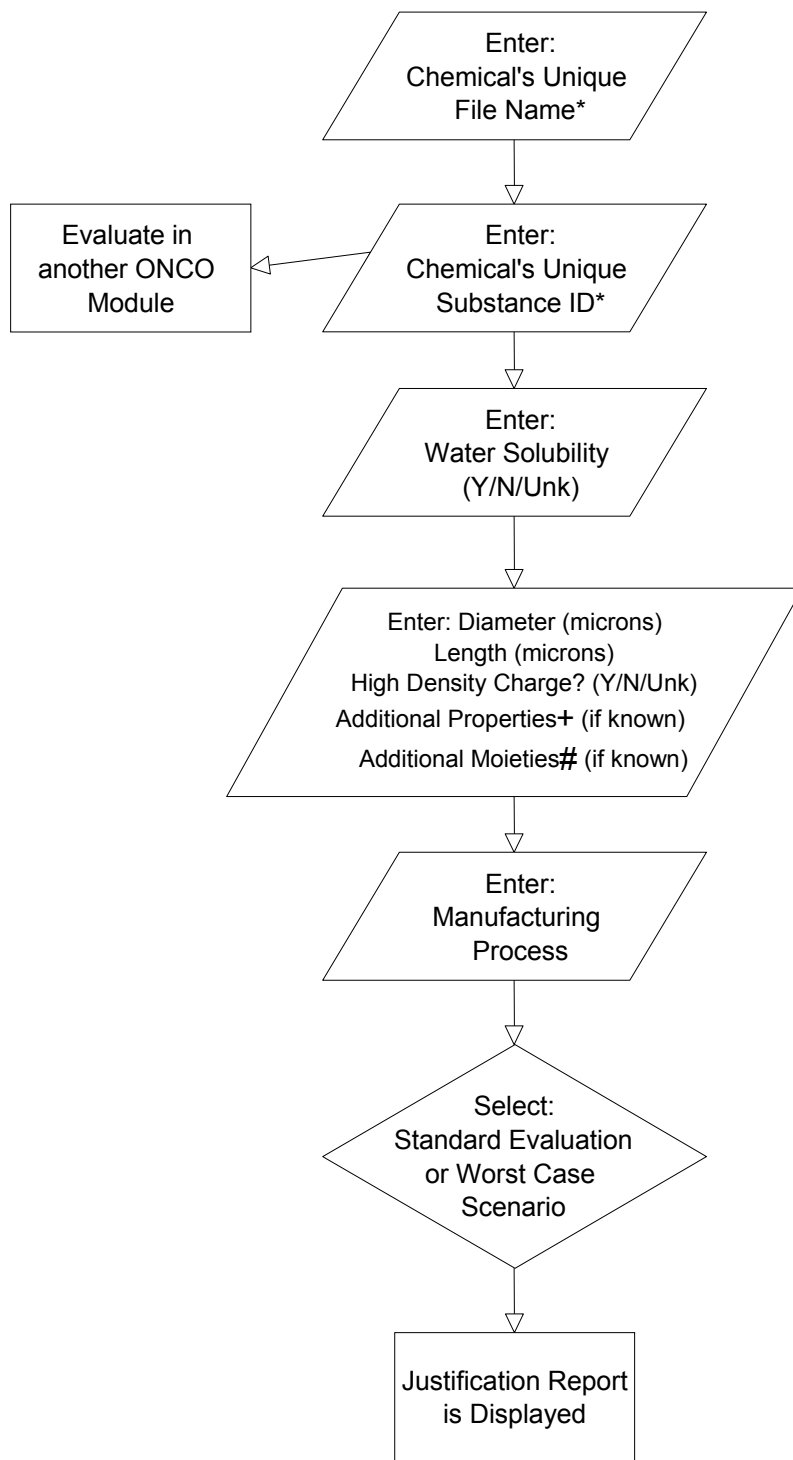
OncoLogic, developed by LogiChem under a cooperative agreement with USEPA, OPPT in support of Sec. 5 of TSCA, can be obtained by contacting: Marilyn S. Arnott, Ph.D., LogiChem, Inc., PO Box 622, Narberth, PA 19072, Email: marnott@ptdprolog.net

Using OncoLogic

Shown on the right is a Flow Diagram for OncoLogic. Each of the 4 modules shown has a detailed flow diagram which is presented on the following pages.



OncoLogic Model Flow Diagram - Fibers



Inputs Needed for Fibers Evaluation:

Water solubility (yes/no)
Diameter (microns)
Length (microns)

Additional Inputs Needed for Refining the Evaluation Are:

Presence of electrical charge
Properties
Flexibility
Durability
In vivo biodegradability
Surface characteristics
Splitting properties
Moieties
High molecular weight polymer
Low molecular weight organic moiety
Metals or metalloids
Manufacturing process
Use scenario

*NOTE: The chemical's file name and substance ID are unique names that the user enters. The chemical's file name is limited to 8 characters. The program will take up to 240 characters for the chemical's substance ID.

Sample Output from OncoLogic Fibers Justification Report

INPUTS:

Chemical file name	= Fiber1	High density charge	= Unk
Substance Id	= Fiber1		
<u>Additional properties:</u>			
Water soluble	= No	Durability	√
Diameter	= 0.1 - 0.5 microns		
Moieties	= none	Median(s)	= 0
Manufacturing process	= Crystallization	Length	= 1 - 3 microns
Scenario evaluation	= Standard	Aspect ratio	= 0

Justification Report is saved in ONCO dir. as ASCII file as "Chemical file name.JST"

RESULTS:**SUMMARY:**

Code Number: Fiber1

Substance Id: Fiber1

The final level of this fiber-type substance is HIGH.

JUSTIFICATION:**STANDARD EVALUATION**

The unifying concept of fiber carcinogenesis is the Stanton Hypothesis. This hypothesis states that the dimensions of a fiber are the major criteria for establishing the concern for its *carcinogenic* potential.

The STANDARD evaluation is the accepted method for determining the *carcinogenic* potential of a fiber. It is based on the median diameter and length. The distribution of dimensions is assumed to be uniform. When a range is entered, the program calculates the median as the average of the high and low values.

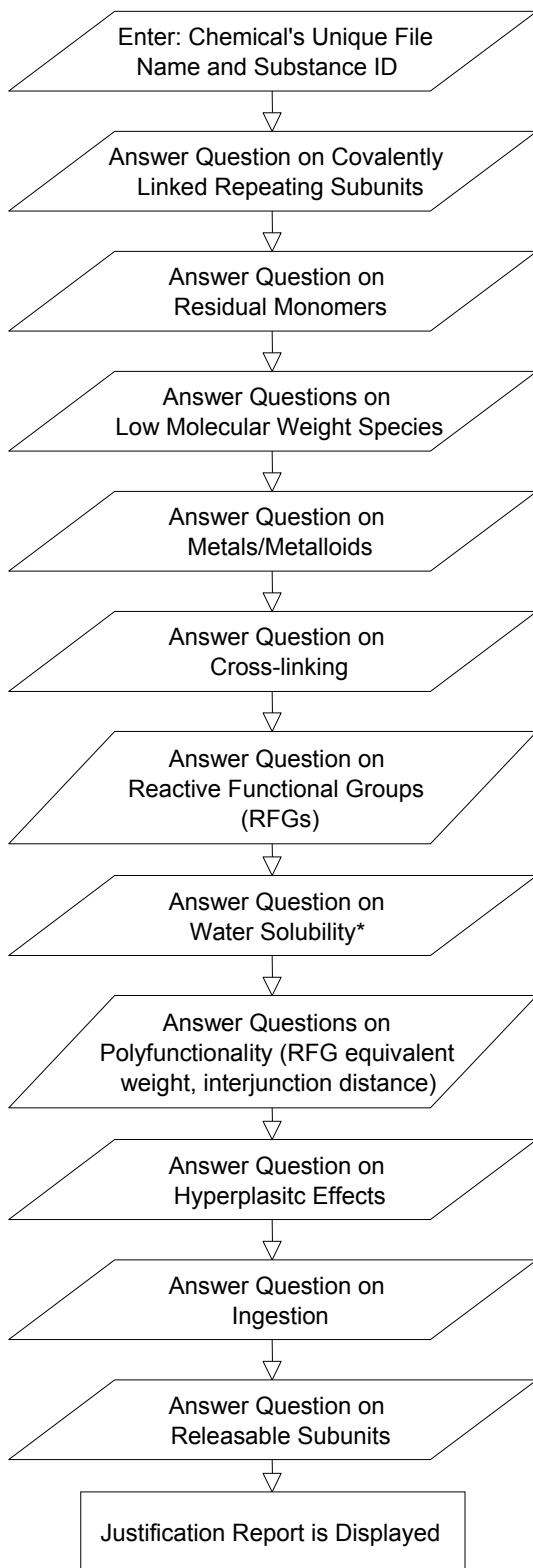
Since the diameter of the fiber is equal to or greater than 0.25 microns and less than 1.5 microns, and its aspect ratio is greater than 5 and not more than 32, the initial level of concern for *carcinogenic* potential of this fiber is MODERATE.

Naturally occurring fibers and synthetic fibers that are manufactured through a crystallization process are assumed to have strong electron donor/basic sites on their surface, since these conditions provide time for orderly build-up of surface structure. This increases the level of concern to HIGH-MODERATE.

The fiber exhibits the following property or properties: durability. These characteristics make minor modifications to the concern level and many are inter-related. Thus, regardless of the number of these characteristics the fiber exhibits, the final level of concern is increased by only one step to HIGH.

The final concern for this fiber-type substance is HIGH.

OncoLogic Model Flow Diagram - Polymers



Inputs Needed for Polymers Evaluation:

Molecular weight
 Water solubility and behavior in water
 Polyfunctional behavior
 Hyperplastic effects
 Possible Ingestion
 Information on chemical structure/properties, including presence of:
 Covalently-linked units
 Residual monomer
 Residual functional groups
 Low molecular weight species
 Metals or metalloids
 Cross-linkages
 Reactive functional groups
 Internal releasable subunits
 Terminal/pendant releasable subunits

*If water solubility is in ppm, convert to percent by dividing the number by 10,000. If water solubility is unknown, enter 0.

Sample Output from OncoLogic Polymers Justification Report

INPUTS:

Chemical file name	=	Polymer1
Substance Id	=	Polymer substance A
Molecular weight	=	1,100
Covalently linked units	=	Yes
Residual monomers >2%	=	No
Low MW species (<500) present	=	Yes
Polymer reactive functional groups (RFGs)	=	Yes
RFGs present	=	Oxygen
Oxygen RFG	=	Epoxide (unsubstituted)
Additional RFGs present	=	No
Metals/Metalloids present	=	No
Crosslinkages present	=	No
Polymer RFGs present	=	Yes
Identify Polymer RFG	=	Oxygen
Oxygen RFG	=	Epoxide (unsubstituted)
Additional RFGs present	=	No
Water solubility as percent weight	=	0.2
Polyfunctional	=	Yes
Functional groups equivalent. wt.	=	550
Interjunction distance	=	Yes
Hyperplastic effects	=	No
Absorption into soft tissue	=	Unknown
Ingestion possible	=	Yes
Internal release subunits	=	No
Terminal pendant subunits	=	No

Justification Report is saved in ONCO directory as ASCII file as "Chemical file name.JST"

RESULTS:**SUMMARY:**

CODE NUMBER: polymer1

SUBSTANCE ID: polymer substance A

The final level of *carcinogenicity* concern for this polymer is LOW MODERATE.

Based on the reactive functional group Epoxide (unsubstituted), the level of concern for the low molecular weight species LOW MODERATE.

CAUTIONARY NOTES:

1. Plasticizers and other additives, if present, should be evaluated separately in the Organics Subsystem.
2. Counterions of polymers with ionic backbones should be evaluated separately.

Continued on next page

Sample Output from OncoLogic Polymers Justification Report

Continued from previous page

JUSTIFICATION:

Because the substance consists of covalently linked repeating units and has a molecular weight greater than or equal to 1000, the substance is classified as a high molecular weight polymer.

Since the polymer contains less than 2% residual monomer(s), the *carcinogenicity* concern for any residual monomers is LOW.

The polymer contains low molecular weight species (>2% below 500), with a reactive-functional-group-bearing sidechain. The level of *carcinogenicity* concern for the low molecular weight species is based on the reactive functional group: Epoxide (unsubstituted).

The level of *carcinogenicity* concern for the low molecular weight species is LOW MODERATE.

The polymer is not cross-linked.

Since the percent water solubility is greater than or equal to 0.1%, the polymer is considered to be soluble in water.

The reactive functional group (RFG) which was used during the evaluation of the polymer is: Epoxide (unsubstituted).

This water soluble polymer is polyfunctional. Based on the expert-assigned inherent *carcinogenic* potential of the RFG(s) that you have entered and the entered information on the functional group equivalent weight of 550 daltons, which is low enough to cause concern, and the interjunction distance of less than ten atoms, which is within the favorable distance for potential cross-linking, the RFG which is retained for the evaluation of the polymer is Epoxide (unsubstituted).

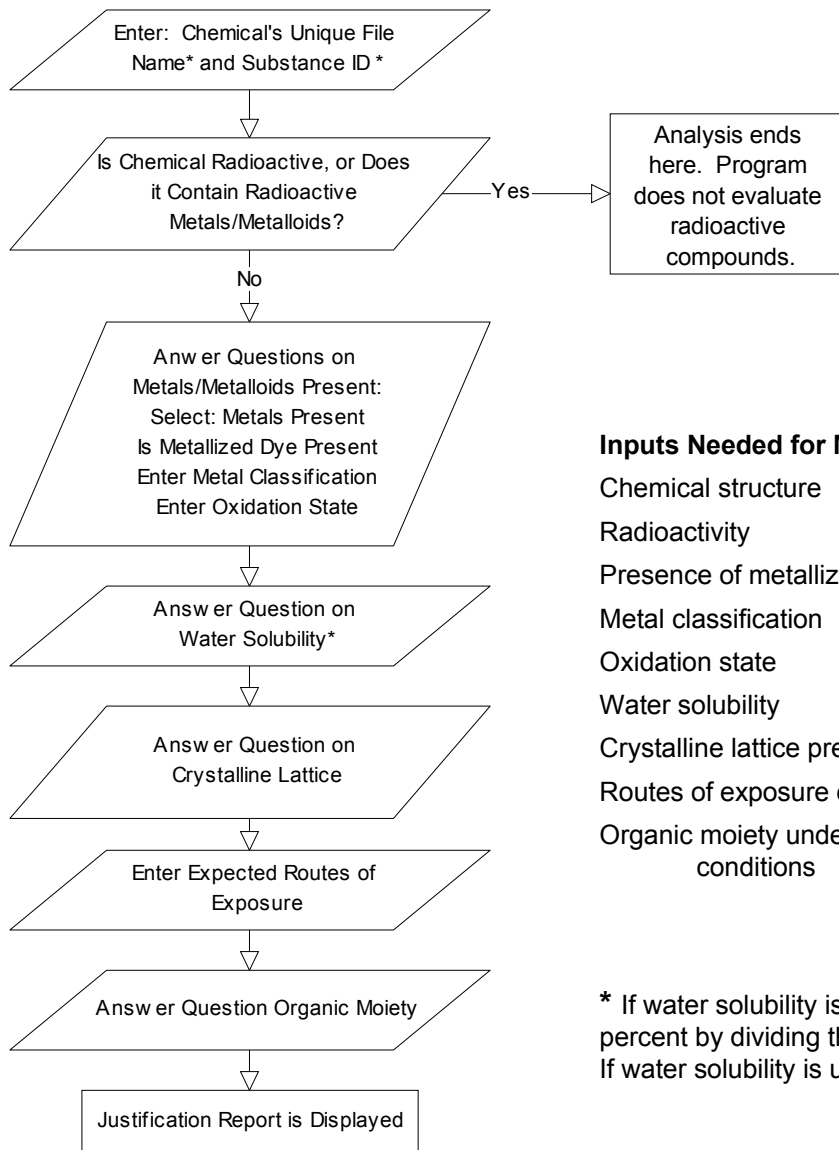
Since this polymer has been demonstrated not to cause (or is not known to have caused) inflammatory and/or hyperplastic changes, *carcinogenicity* concerns arising from these pathophysiological changes can be eliminated.

The RFG which is contained in this polymer is known to be stable in solution or as an emulsion in water. The current level of *carcinogenicity* concern based on the RFG is retained.

The water soluble polymer has a molecular weight less than or equal to 5,000. The polymer contains reactive-functional-group-bearing sidechains but has not (or is not known to have) demonstrated an ability to be absorbed and to accumulate in soft tissue. Therefore, the level of *carcinogenicity* concern for this polymer is LOW MODERATE.

The final concern for this polymer is LOW MODERATE.

OncoLogic Model Flow Diagram - Metals



Sample Output from OncoLogic Metals Justification Report

INPUTS:

Chemical file name	=	Crystal	Oxidation state	=	Hexavalent
Substance Id	=	Crystal	Water solubility	=	Sparingly soluble
Radioactivity	=	No	Crystalline lattice	=	Yes
Metals present	=	Cr and Zr	Route of exposure	=	Inhalation
Metallized dye or pigment	=	No	Organic moiety	=	No
Metal classification	=	Inorganic or other comp.			

Justification Report is saved in ONCO directory as ASCII file as "Chemical file name.JST"

RESULTS:

Code Number: crystal
Substance Id: crystal

SUMMARY:

The final level of concern for this Cr-containing inorganic or organic compound, when the anticipated exposure is via the inhalation route, is HIGH.

JUSTIFICATION:

Since this substance contains more than one metal, Cr, Zr, the system has considered all metals present. The level of concern and the line of reasoning are based on the metal which provides the highest level of *carcinogenicity* concern. When more than one metal gives the same highest level of concern, the line of reasoning is given for only one of the metals.

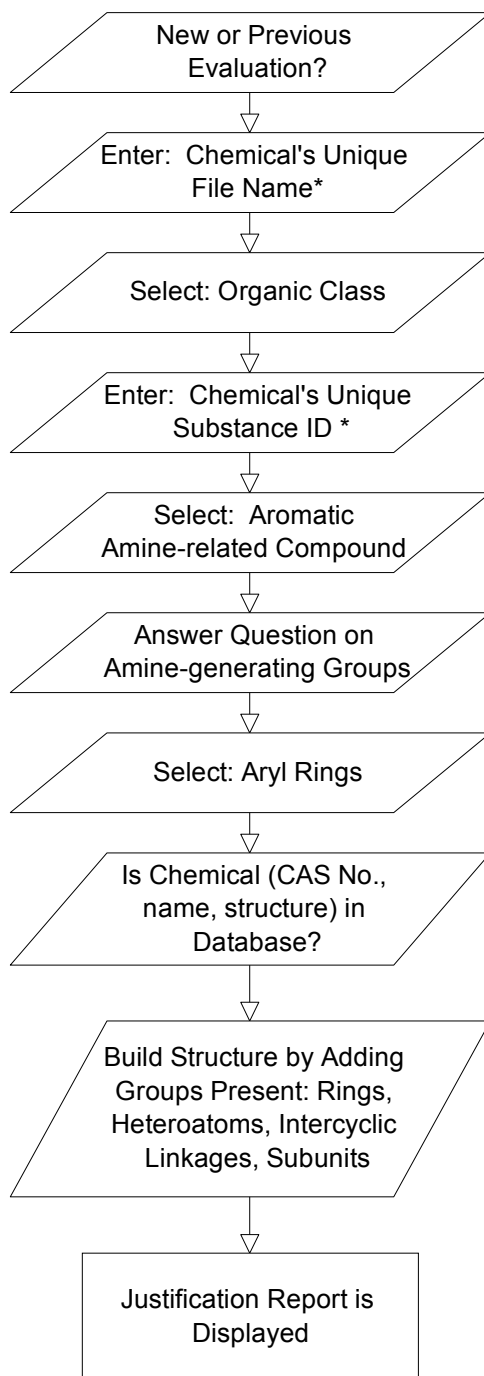
In general, virtually all Cr-containing compounds are of some *carcinogenicity* concern unless they can be clearly shown to be not bioavailable. Exposure to these compounds by inhalation or injection is of greater concern than exposure by the oral or dermal route.

The *carcinogenic* potential of inorganic chromium compounds is affected by their oxidation state, crystallinity, and solubility, which affect the extent of compound uptake by cells. Hexavalent compounds are more easily taken up by cells than trivalent; and crystalline compounds are more easily taken up than amorphous compounds. Sparingly soluble and insoluble compounds are more likely than soluble compounds to be retained at the site of exposure, and thus have more of an opportunity to be taken up by the cells. Organic chromium compounds containing a Cr-C covalent bond are treated as inorganic compounds because the Cr-C covalent bond is expected to be easily hydrolyzed in aqueous solution.

Since the substance is a(an) inorganic or organic compound, and the oxidation state of chromium is hexavalent, and exposure to this sparingly soluble, crystalline substance is expected to be by the inhalation route, the level of *carcinogenicity* concern is HIGH.

The final level of concern for this Cr-containing inorganic or organic compound, when the anticipated exposure is via the inhalation route, is HIGH.

OncoLogic Model Flow Diagram - Organics



Inputs Needed for Organics Evaluation:

Organic chemical class

CAS number/Chemical name (if listed)

Molecular structure, including presence of:

Rings

Functional groups

Linkages

Substituents

NOTE:

*The chemical's file name and substance ID are unique names that the user enters. The chemical's file name is limited to 8 characters. The program will take up to 240 characters for the chemical's substance ID.

Sample Output from OncoLogic Organics Justification Report

INPUTS:

Chemical file name = Amine1

Organic class = Aromatic amine

Substance Id = Aromatic amine#1

Aromatic-related compound class = None

Amine-generating group = Yes

Aryl rings selected:

6-member rings = 1

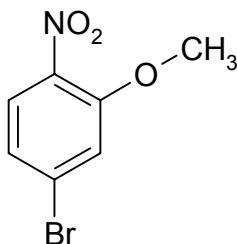
Heteroatoms = No

Answers are correct

Structure building:

Select:

- Build
- Add
- Substituents
- Alkoxy (-OCH₃)
- Amine-generating group (NO₃)
- Other (Br)

RESULTS:

Justification Report is saved in ONCO directory as ASCII file as "Chemical file name.JST"

SUMMARY

Code Number: Amine1

Substance Id: Aromatic Amine#1

The level of carcinogenicity concern for this compound is HIGH-MODERATE.

JUSTIFICATION:

In general, the level of carcinogenicity concern of an aromatic amine is determined by considering the number of rings, the presence or absence of heteroatoms in the rings; the number and position of amino groups; the nature, number and position of other nitrogen-containing 'amine-generating groups;' and the type, number and position of additional substituents.

Aromatic amine compounds are expected to be metabolized to N-hydroxylated/N-acetylated derivatives which are subject to further bioactivation, producing electrophilic reactive intermediates that are capable of interaction with cellular nucleophiles (such as DNA) to initiate carcinogenesis.

Nitro groups of aryl compounds can be reduced by nitro reductase to amino groups yielding aromatic amine compounds. The evaluation of this compound proceeds as if the nitro group were a free amine group.

An aromatic compound containing one benzene ring, one amino group, and one methyl or methoxy group ortho- to the amino group, has a carcinogenicity concern of HIGH-MODERATE.

The additional chloro and/or bromo group(s) generally raise(s) the level of concern, but they also impose an upper limit of HIGH-MODERATE on the concern level of the compound. Therefore, the level of concern remains HIGH-MODERATE.

The final level of carcinogenicity concern for this compound is HIGH-MODERATE.

Screening for Non-cancer Human Health Effects in the Absence of Data

The P2 Framework models predict aquatic hazard (ECOSAR and the PBT Profiler), cancer hazard potential of chemicals (OncoLogic), and identify structures present described in EPA's Chemical Categories (PBT Profiler). As currently constructed, the does not address all biological endpoints. The "Screening for Non-cancer Human Health Effects" protocol is provided as one method for screening chemicals of concern for non-cancer health effects in the absence of data. The protocol adheres to the scientifically accepted data hierarchy, and follows that used by EPA's Risk Assessment Division in the estimation of non-cancer health effects of PreManufacture Notices (PMNs) under TSCA. As described in an earlier section of this manual, EPA has more than 20 years experience reviewing chemicals in the absence of data.

Data Hierarchy

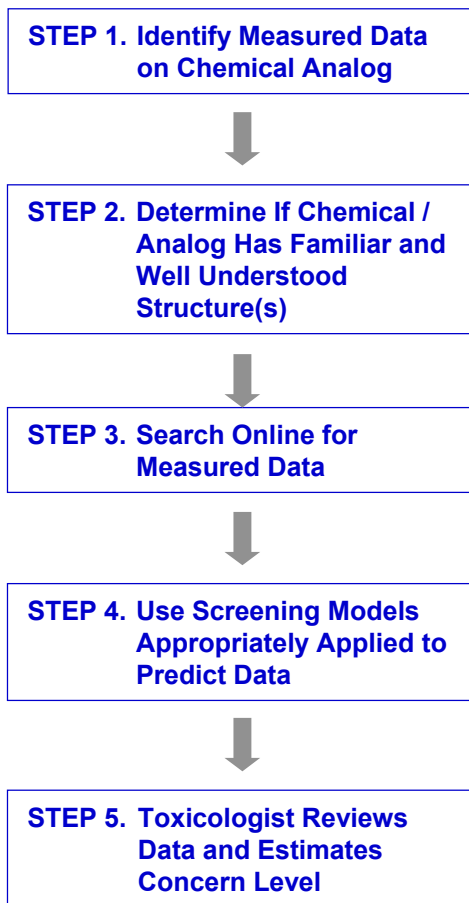
- ★ ★ ★ Highest Quality: Validated measured data from a well designed laboratory study are always preferred.
- ★ ★ Analog Data: When data are not available, data on a close analog may be used. Analog must be identified by a qualified chemist.
- ★ Predicted Data: If no data on the chemical or the analog can be located, data may be predicted by appropriately using scientifically sound models.

If Testing Becomes Necessary

If measured data are not available, predictive models can not be used, and a decision is made to conduct testing, the screening process described here can help identify the most relevant properties, effects, and exposures, and help determine which tests may be necessary to fully characterize the chemical(s). When deciding on testing, or reviewing test data, consideration should be given to the test species, route of exposure, and quality of the data. Information on these aspects can be found in OPPTS' harmonized test guidelines developed for testing chemicals under TSCA and Federal Insecticide and Rodenticide Act (FIFRA) www.epa.gov/opptsfrs/home/testmeth.htm Relevant guidelines include: #835 (Fate, Transport and Transformation), #850 (Ecological Effects), #870 (Health Effects), and 880 (Biochemicals). Additional reliable test guidelines are the Organization for Economic Cooperation and Development (OECD) Screening Information Data Sets (SIDS), which are described at www1.oecd.org/ehs/guide/index.htm and www.epa.gov/chemrtk/sidsappb.htm. When characterizing potential risk of the chemical of concern, EPA's Risk Assessment Guidelines (located at <http://www.epa.gov/ncea/rafpub.htm>) can provide information on assessing risk.

Screening for Non-cancer Human Health Effects

The steps in this protocol are illustrated to the right.



Screening for Non-cancer Human Health Effects in the Absence of Data

STEP 1. Locate Measured Data on Chemical / Analog

Data on the following properties should be located. Suggested data sources are included in Appendix B of this document.

- ❖ Physical / Chemical Properties
- ❖ Fate Properties
 - Biodegradation
 - Media half-lives
 - Metabolites/break down products
- ❖ Biochemical Transformation Potential
 - Reaction intermediates or reaction products
- ❖ For Polymers
 - Number average molecular weight
 - % below MW of 500 and % below MW of 1,000
 - MW distribution, if available
- ❖ For Surfactants
 - Cmc and Krafft temperature (ambient conditions)
- ❖ For Solids
 - Particle size distribution
 - Melting point
- ❖ Aquatic Toxicity: Chronic and acute toxicity to fish, invertebrates, algae

STEP 2. Determine If Chemical / Analog Has Familiar and Well Understood Structure(s)

- ❖ Check whether chemical belongs to one of EPA's New Chemicals Program Chemical Categories, available at www.epa.gov/oppt/newchemicals/chemcat.htm
- ❖ Chemicals Causing Local Effects are listed in Appendix D. Chemicals Causing Systemic Effects are listed in Appendix E. (Lists are not intended to be exhaustive.)
- ❖ Polymers (high MW chemicals) may not be toxic to fish as they are often too large to cross most biological membranes, however certain types of polymers may present human health concerns. EPA has concern for three types of polymers with MW >10,000. These are (a) soluble, (b) insoluble/non-water absorbing ("non-swellable"), and (c) water absorbing ("swellable"), describes at www.epa.gov/opptintr/newchemicals/hmwtpoly.htm and included in Appendix F.

STEP 3. Search Online for Measured Data

Measured data may be available in reference or online sources. The source of any data submitted should be provided. The test species and test quality should be considered as well. There are many reference and online sources of human health effects data. Appendix B provides reference and online data sources, however, these lists are not intended to be exhaustive. Readers are encouraged to conduct their own online searches.

STEP 4. Use Screening Models, Appropriately Applied, to Predict Data

Many screening models are available that predict human health effects. One online aid to identifying appropriate models that predict the desired endpoints is OECD's Database on Chemical Risk Assessment Models at <http://webdomino1.oecd.org/comnet/env/models.nsf>.

Before any screening model is used, it is essential that the assessor determine the appropriateness of that specific model for evaluating the chemical(s) of concern. Not all models can evaluate all classes of chemicals. In addition, model results must be interpreted with caution. Consult the specific model's User Guide for information on appropriately using the model, and always provide the specific model used to predict the properties and effects submitted.

Once the appropriate models have been identified, and the chemical has been evaluated, the predictions should be evaluated carefully. Once this has been done, the assessor can summarize the significance of potential hazards.

Screening for Non-cancer Human Health Effects in the Absence of Data

STEP 5. Toxicologist Reviews Data and Estimates Concern Level

An experienced toxicologist should review the predicted data and set a concern level. Following is general guidance for setting concern levels, used by EPA in screening new chemicals under TSCA:

❖ HIGH CONCERN

- Evidence of adverse effects in humans
- Conclusive evidence of severe effects in animal studies

❖ MODERATE CONCERN

- Suggestive animal studies
- Analogue data
- Chemical class known to produce toxicity

❖ LOW CONCERN

- No concern identified

ECOSAR to Estimate Aquatic Toxicity

What Does the ECOSAR Model Do?

ECOSAR (Ecological Structure Activity Relationships) estimates the aquatic toxicity of a chemicals used in industry and discharged into water. The program uses Structure Activity Relationships (SARs) to estimate a chemical's acute (short-term) toxicity and, when available, chronic (long-term or delayed) toxicity. ECOSAR can predict the potential toxicity of the chemical to plant and animal live in the water body. The model uses measured data to predict toxicity of chemicals lacking data.

How are the model predictions useful in risk assessment?

An understanding of the chemical's aquatic toxicity helps the risk assessor estimate if the release of the chemical will adversely affect aquatic biota and the aquatic ecosystem.

Inputs

CAS number or chemical structure in SMILES notation, log KOW predicted by ClogP*, and measured values for log Kow, WS, and MP should be entered if available. *ClogP predictions of log KOW should be entered because most SARs in ECOSAR were developed using KOW values predicted using ClogP. ClogP is a program developed by BioByte (www.biobyte.com). ClogP values are fairly consistent with EPI Suite™ values, however, ClogP values should be entered if available. All SARs in ECOSAR are being recalculated using EPI Suite™ log Kow values.

Outputs

Acute (48-hr or 96-hr) and Chronic (14-day, 16-day, or 30-day) values in mg/L (ppm) for fish, invertebrate (Daphnids), and green algae are provided. SAR Chemical Class is given. Log Kow cutoff values for the SARs used are provided so that the user can determine if the values are reliable. If the chemical is not soluble enough to reach effects concentrations (referred to as “No Effects at Saturation or NES”) this is also indicated.

Saving Output

Results can be printed when displayed. After results are displayed click on “Save Results” and you can save results as a “.dat” file that can be opened using MSWord or WordPerfect. Output can also be copied (click on “Copy”) through the Windows Clipboard. Structures can be saved as an ISIS “.skc” file or through the Windows Clipboard. Further explanations are in “Help” on the Results page.

Important Notes

- ❖ ECOSAR users should have some knowledge of environmental toxicology and organic chemistry.
- ❖ The current version of ECOSAR can not be used to estimate toxicity of certain chemical classes, for example: charged dyes, polymers, inorganics, or organometallics.
- ❖ The latest version of ECOASR – the “G” version – is incorporated into the EPI Suite™ of models.
- ❖ The “HELP” screens in ECOSAR contain useful information, including:
 - Help writing SARs
 - SAR equations
 - List of SARs programmed into ECOSAR
 - ECOSAR Chemical Class List

Where Can I Get ECOSAR?

The latest version of ECOSAR (v.099g) can be downloaded at no cost from EPA, OPPT New Chemicals Program web site: <http://www.epa.gov/oppt/newchems/21ecosar.htm> This version of ECOSAR has been incorporated into the EPI Suite™.

ECOSAR User Manual, “ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals (EPA-748-R-93-002), and Estimating Toxicity of Industrial Chemicals to Aquatic Organisms Using Structure Activity Relationships” (EPA-748-R-93-001). For a copy contact EPA’s National Center for Environmental Publications and Information 800-490-9198, www.epa.gov/ncepihom/index.htm

ECOSAR to Estimate Aquatic Toxicity

Ecosar v0.99g

File Edit Functions BatchMode ShowStructure Special_Classes Help

Previous Get User Save User CAS Input Calculate

Enter SMILES:

Enter NAME:

CAS Number:

Chemical ID 1:

Chemical ID 2:

Chemical ID 3:

Log Kow:

Inputs:

CAS 108-88-3

Melting Pt 25.0

WS 573.1

Log Kow 2.540 (ClogP)

Measured Log KOW 2.73

Measured Water Sol (mg/L):

Melting Point (deg C):

Measured Log Kow:

Either the structure in SMILES or the CAS number must be entered to run the program.

Ecowin Results

Print Save Results Copy Remove Window Help

SMILES : c(cccc1)(c1)C

CHEM : Benzene, methyl-

CAS Num : 000108-88-3

ChemID1:

ChemID2:

ChemID3:

MOL FOR: C7 H8

MOL WT : 92.14

Log Kow: 2.54 (User entered)

Melt Pt: 25.00 deg C

Wat Sol: 573.1 mg/L (measured)

ECOSAR v0.99g Class(es) Found

Neutral Organics

ECOSAR Class Organism Duration End Pt mg/L (ppm)

=====

Neutral Organic SAR : Fish 14-day LC50 41.891

(Baseline Toxicity)

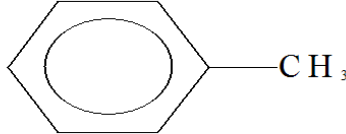
Neutral Organics : Fish 96-hr LC50 21.225

Neutral Organics : Fish 14-day LC50 41.891

Neutral Organics : Daphnid 48-hr LC50 23.608

Structure

The structure is shown in a separate window and can be saved as a MOL file.



Benzene, methyl-

The results may be Printed, Saved to a file, or Copied to the Windows clipboard and pasted into another Windows Program, such as MS Word.

ECOSAR to Estimate Aquatic Toxicity

Results from the ECOSAR Model

SMILES : c(cccc1)(c1)C
 CHEM : Benzene, methyl-
 CAS Num: 000108-88-3
 ChemID1:
 ChemID2:
 ChemID3:
 MOL FOR: C7 H8
 MOL WT : 92.14
 Log Kow: 2.54 (User entered)
 Melt Pt: 25.00 deg C
 Wat Sol: 573.1 mg/L (measured)

Standard toxicity profile used by EPA for freshwater species (mg/L or ppm):

Acute effects	Duration	Endpoint
fish	96-h	LC50
daphnid	48-h	LC50
green algae	96-h	EC50
Chronic effects	Duration	Endpoint
fish	30-d	ChV
daphnid	16-d	EC50 or ChV
green algae		ChV

ECOSAR v0.99g Class(es) Found
 Neutral Organics

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organic SAR (Baseline Toxicity)	: Fish	14-day	LC50	41.891
Neutral Organics	: Fish	96-hr	LC50	21.225
Neutral Organics	: Fish	14-day	LC50	41.891
Neutral Organics	: Daphnid	48-hr	LC50	23.608
Neutral Organics	: Green Algae	96-hr	EC50	15.225
Neutral Organics	: Fish	30-day	ChV	2.983
Neutral Organics	: Daphnid	16-day	EC50	1.533
Neutral Organics	: Green Algae	96-hr	ChV	2.080
Neutral Organics	: Fish (SW)	96-hr	LC50	6.313
Neutral Organics	Mysid Shrimp	96-hr	LC50	4.163

mg/kg (ppm)
 dry wt soil

H-M-L Levels (mg/L or ppm)

ACUTE

CHRONIC

High < 1

High < 0.1

Mod. = 1 - 100

Mod. = 0.1 - 10

Low > 100

Low > 10

Notes: Chemical may not be soluble
 at this predicted effect.
 Acute toxicity log Kow cutoff: 5.0
 Chronic toxicity log Kow cutoff: 6.4
 Chronic toxicity log Kow cutoff: 8.0

MW cutoff: 1000

These SARs are not valid
 at higher
 cutoff

Setting concern levels:

High Concern = Any Acute value < 1 mg/L Chronic < 0.1 mg/L)

Mod. Concern = Lowest of the 3 is > 1 and < 100 mg/L (Chronic > 0.1 and < 10.0 mg/L)

Low = All 3 are > 100 (Chronic > 10.0 mg/L), or there are No Effects at Saturation (occurs when water solubility of the chemical is higher than an effect concentration).

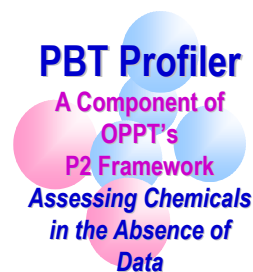
Interpreting the Results from ECOSAR

Determining concern concentration (CC): CC is the lowest ChV divided by an uncertainty factor (assessment or safety factor) of 10. In order to be conservative and because the uncertainty (or assessment) factor is one significant digit, the CC will be rounded up to be one significant digit e.g., a CC of 175 will be rounded up to 200.

PBT Profiler – Estimations of Persistence, Bioaccumulation, and Toxicity

What Does the PBT Profiler Model Do?

The PBT Profiler is a no cost, online PBT screening methodology. It estimates environmental persistence (P), bioconcentration potential (B), and aquatic toxicity (T) of discrete chemicals based on their molecular structure. It is Internet-based and there is no cost for use. When the user accesses the PBT Profiler on the Internet, the program prompts the user to enter the CAS Registry Numbers (RNs) of chemicals under consideration. The PBT Profiler is linked to a database containing the CAS RNs and the associated chemical structures for over 100,000 discrete chemical substances. If the CAS RN is in the database, the PBT Profiler will translate the CAS RN into a chemical structure, predict the PBT characteristics, and provide a PBT profile in an easy to understand format. A drawing program is available so that the user can draw and enter the structure if the CAS RN is not in the database. The structure can also be entered as a SMILES Notation. The PBT Profiler compares the results of a profile with the PBT criteria established for Premanufacture Notices (PMNs) submitted under section 5 of TSCA; and the final rule for reporting chemicals under the Toxic Chemical Release Inventory (TRI), under section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA).



How are the model predictions useful in risk assessment?

Persistent, bioaccumulative, and toxic pollutants (PBTs) are highly toxic, long-lasting substances that can build up in the food chain to levels that are harmful to human and ecosystem health. They are associated with a range of adverse human health effects, including effects on the nervous system, reproductive and developmental problems, cancer, and genetic impacts.

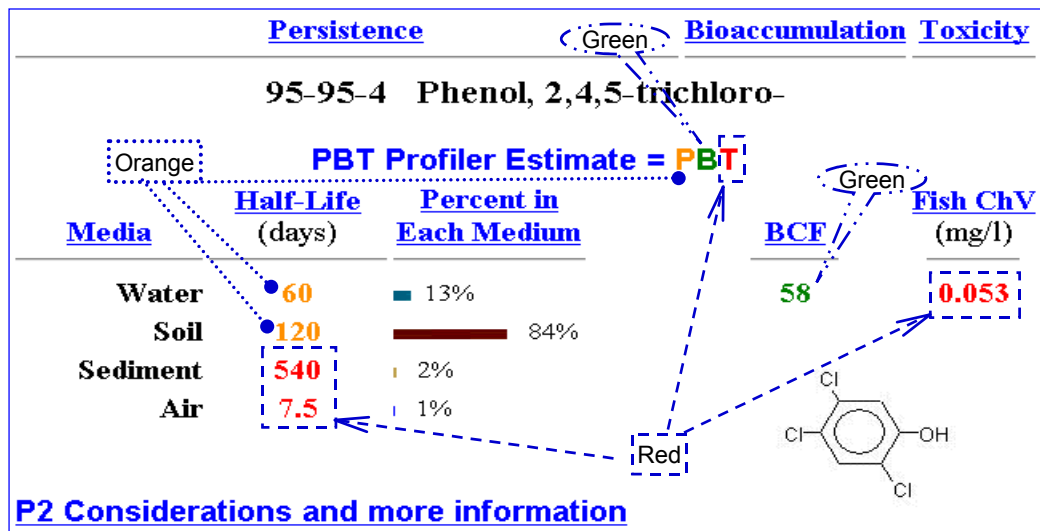
Inputs

- ❖ CAS number or chemical structure in SMILES notation
- ❖ Structure can be drawn using an integrated drawing program

Outputs

A sample output showing the three tiers of output is provided below. Each tier increases in detail. These three levels are:

- 1. PBT Summary** given in a color coded format, with green indicating no criteria exceeded, orange indicating criteria are exceeded, and red indicating criteria are greatly exceeded. If P, B, AND T are any combination of red or orange the chemical may be a PBT. In the example below, trichlorophenol, which is **PBT**, P is orange, B is green, and T is red, is not a potential PBT.
- 2. Detailed Results** which gives % in each media, media half-lives; BCF; and fish chronic toxicity.
- 3. P2 Considerations and More Information** is a link to additional detailed information on the chemicals predicted environmental fate, BCF, and toxicity that can be useful for the management of the release of the chemical to the environment and to control exposures and potential risk.



PBT Profiler – Estimations of Persistence, Bioaccumulation, and Toxicity

Examples of PBT Summary Predicted Values

CAS RN	Chemical	PBT Summary	
50-01-1	Guanidine hydrochloride	PBT	(not a potential PBT)
447-53-0	1,2-Dihydro-naphthalene	PBT	(not a potential PBT)
95-95-4	2,4,5-Trichloro-phenol	PBT	(not a potential PBT)
8001-35-2	Toxaphene	PBT	(a presumptive PBT*)

*Note: Toxaphene, and other chemicals is listed as PBTs in EPA's final rule on Persistent, Bioaccumulative, and Toxic Substances, are flagged by the PBT Profiler, and the user is advised that this chemical has been listed as a PBT by EPA.

Criteria Used by The PBT Profiler

Persistence and Bioaccumulation criteria are based on EPA policy statements published in the Federal Register:

- ❖ New PBT category for PMNs submitted under TSCA sec. 5
- ❖ Final rule concerning reporting under Toxics Release Inventory (TRI) under sec. 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA):
 - Adding several PBTs to the list of those requiring reporting
 - Lowering reporting thresholds for certain PBTs already on TRI. The PBT profiler uses a different set of criteria to highlight chemicals that may be toxic.

Toxicity Criteria are those used by EPA's New Chemical Program for Fish Chronic toxicity. Potential human toxicity is identified based on Chemical Categories. If the chemical being screened has structures identified and described in this document, the human health concerns of those structures are provided in the results screen.

CRITERIA used by The PBT Profiler			
PERSISTENCE	Not Persistent	Persistent	
Water, soil, sed.*	< 60 d	≥ 60 d	> 180 d
Air^	≤ 2 d	> 2 d	
BIOACCUMULATION	Not Bioaccum.	Bioaccumulative	
Fish BCF*	< 1,000	≥ 1,000	≥ 5,000
TOXICITY	Not Toxic	Toxic	
Fish ChV*	> 10 mg/L or No Effects at Saturation	10 – 0.1 mg/L	< 0.1 mg/L
EPA Criteria: *New Chemical Program, ^TRI			

Important Notes

- ❖ The PBT Profiler online site www.pbtprofiler.net provides hot links to help which explain Methodology, Criteria, Security, Interpreting Results, Examples of Chemicals to run, Chemicals that Should not be Profiled (and the reasons why these chemicals are not appropriate for the Profiler, Limitations,
- ❖ Many chemicals can be run in one session by entering the chemicals sequentially.
- ❖ For technical reasons, there are certain classes of chemicals that should not be profiled using the PBT Profiler. Check the online site for more information. The chemicals are:
 - Chemicals with Experimental Data
 - Inorganic Chemicals
 - Reactive Chemicals
 - Salts (Organic Salts)
 - High Molecular Weight Compounds
- Chemicals with Unknown or Variable Composition
- Mixtures
- Surfactants
- Highly Fluorinated Compounds

Where Can I Get The PBT Profiler?

The model can be accessed using a web browser and used online at www.epa.gov/opptintr/pbtprofiler/
 The PBT Profiler can not be downloaded and used on a PC. Information on the PBT Profiler is available at www.epa.gov/opptintr/pbtprofiler/

PBT Profiler – Estimations of Persistence, Bioaccumulation, and Toxicity

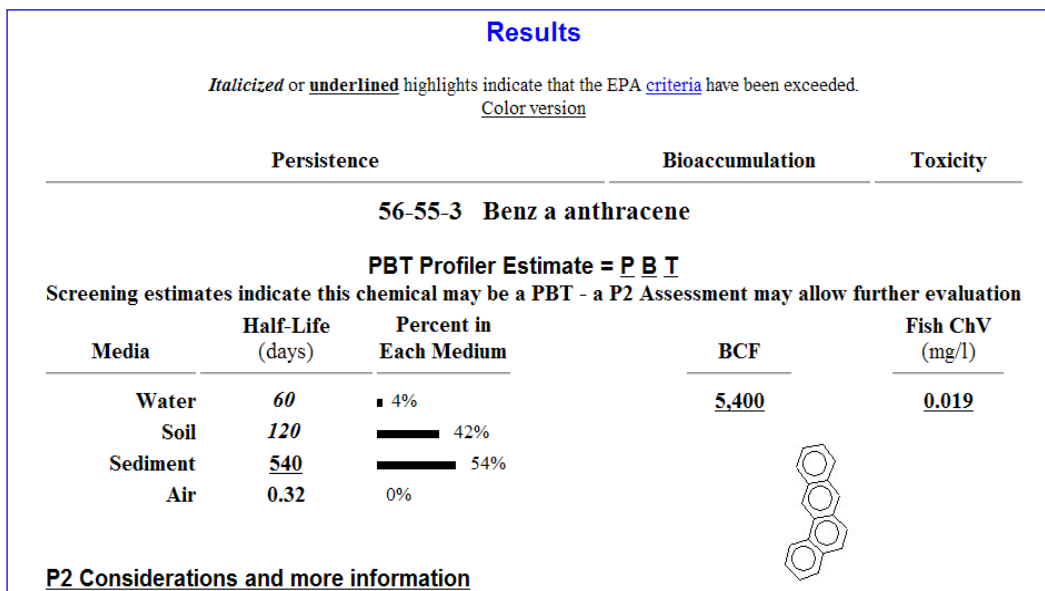
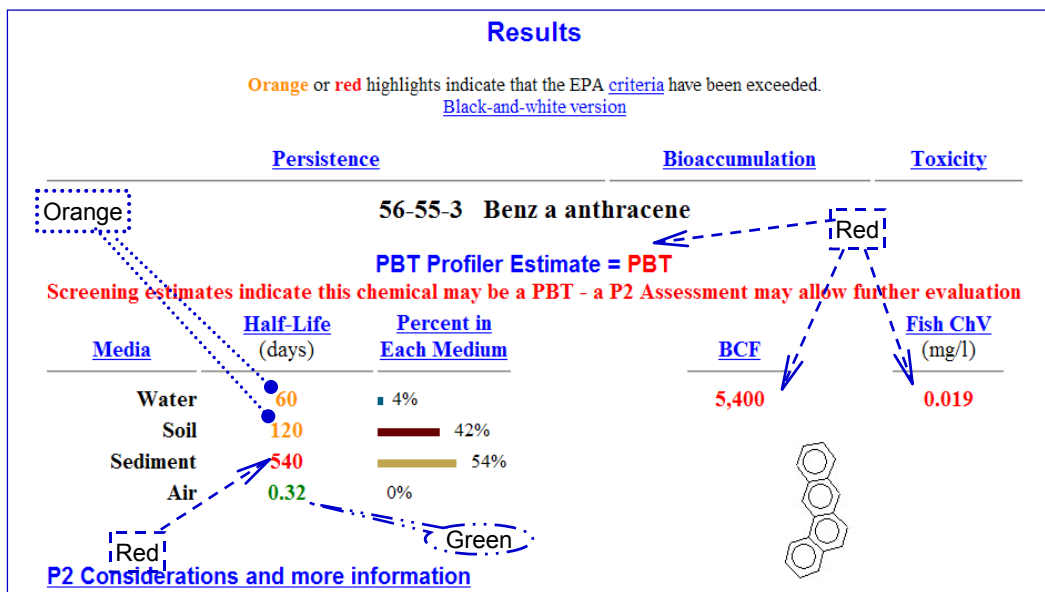
Saving Output

Print Results screens on a color printer, or copy and paste (“Block”, “Copy”, and “Paste”) into MSWord.

Sample Output From The PBT Profiler

A sample model run from the PBT Profiler of a known PBT chemical Benz a anthracene (CAS 56-55-3) is shown below printed in the color version, and in a black & white (B&W) version. Users can toggle between the color and B&W version.

The B&W version was created because not everyone has access to a color printer, and some people do have color-weak vision. Results in red (criteria greatly exceeded) in the Black & White version are **bold and underlined**. Results in orange (criteria exceeded) in the B&W version are *italicized*. Results in green (no criteria exceeded) are in normal font.



Models to Estimate Exposure and/or Risk

The EXPOSURE/RISK MODELS included in this section are:

- ❖ E-FAST - Exposure, Fate Assessment Screening Tool
- ❖ ChemSTEER - Chemical Screening Tool for Exposure and Environmental Releases

Following are brief fact sheets providing information on the models OPPT developed and uses to estimate the risk to receptors from exposure to chemicals released to the environment. Information provided on each model includes:

- ❖ What exposure/risk property does the model estimate?
- ❖ What is significant about the exposure/risk property to exposure assessment?
- ❖ Why is knowing the exposure/risk property important?
- ❖ Why would I want to use the model?
- ❖ What do I need to run the model?
- ❖ What are the inputs and outputs for the model?

Exposure, Fate Assessment Screening Tool (E-FAST)

What Does the E-FAST Model Do?

E-FAST is a Windows based model that incorporates previous DOS based screening level exposure models: SEAS, PDM3, Dermal, and SCIES. E-FAST also incorporates the DOS model FLUSH, which was not previously a part of the P2 Framework. E-FAST provides screening-level estimates of:

- ❖ Concentrations of chemicals released to air, surface water, landfills, and from consumer products.
- ❖ Potential inhalation and ingestion dose rates resulting from these releases.
- ❖ Concentrations and doses are designed to reasonably overestimate exposures, for use in screening level assessment.

How are the model predictions useful in risk assessment?

Knowing the amount of a chemical released to air, landfills, and surface water will help the risk assessor determine if the chemical may pose a health threat to humans or the aquatic ecosystem.

Inputs: Chemical structure (entered as CAS RN and retrieved from the accompanying SMILECAS database; SMILES notation; or drawn and saved as MDL). This program can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. Available measure data should be entered as well.

Outputs:

- ❖ Molecular weight and formula
- ❖ Water solubility at 25°C (milligrams per liter)
- ❖ Chemical structure can be printed or saved as either MDL ISIS SKC file or MDL MOL file

Important Notes

E-FAST HELP has information on:

- ❖ Getting Started
- ❖ Input Pages for all modules
- ❖ Results Pages for all modules
- ❖ References

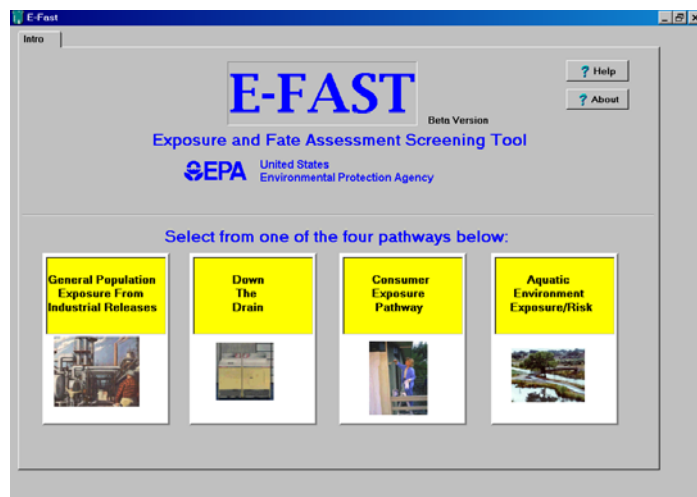
E-FAST is Organized Into 4 Modules:

1. General Population Exposure from Industrial Releases (Formerly the model SEAS)
2. Down-the-Drain Residential Releases (Formerly the model FLUSH, which was not previously part of the P2 Framework)
3. Consumer Exposure Pathway (CEM) (Formerly the models SCIES and Dermal)
4. Aquatic Environment Exposure / Risk (Formerly the model PDM3)

Where Can I Get E-FAST?

The E-FAST Model and documentation manual can be downloaded from the Internet at:

<http://www.epa.gov/opptintr/exposure>



E-FAST: General Population Exposure from Industrial Releases

Inputs

General Release Information

- ❖ Release activity (i.e. Industrial Use, Processing);
- ❖ Number of sites being assessed;
- ❖ Release media – 4 types are modeled: surface water, landfill, ambient air via incineration, and ambient air via fugitive release;
- ❖ Release amounts and frequency for each media;
- ❖ For surface water releases the user will need to determine if the analysis will be site specific or generic (using SIC codes).

Physical Chemical Properties

- ❖ Bioconcentration Factor (BCF);
- ❖ Concentration of Concern (CC);

Exposure Factors

- ❖ This module has a default exposure factors for adults, children, and infants (All of the factors can be revised if necessary).

Fate Properties

- ❖ Wastewater treatment removal;
- ❖ Drinking water treatment removal;
- ❖ Percent removal during incineration;
- ❖ Groundwater migration potential.

Outputs

Human Exposure

- ❖ Drinking water exposure from surface water releases;
- ❖ Fish ingestion exposure from surface water releases;
- ❖ Inhalation exposure from fugitive releases;
- ❖ Inhalation exposure from incineration releases;
- ❖ Drinking water exposure from landfill releases.

Aquatic Environment

- ❖ Post-treatment concentration in surface water;
- ❖ Days per year the COC is exceeded;
- ❖ Percentage of the year the COC is exceeded.

Date Entry Screen

E-FAST

Intro General Pop Exp

This is the starting page for the General Population Exposure From Industrial Releases Module. In this page, you must input a chemical ID. You must choose from at least one of the check boxes, indicating the type of release activities that are being performed. Next to each check box, you must input the number of scenarios that correspond to the selected release. Once you are finished inputting your selections here, press the "continue" button at the bottom of this screen.

Chemical ID: sample

Make Selections From the General Population Exposure Screen

	# Scenarios
<input type="checkbox"/> Manufacturing	0
<input type="checkbox"/> Processing	0
<input type="checkbox"/> Industrial Use	0
<input type="checkbox"/> Commercial Use	0
<input type="checkbox"/> Other	0

Continue

Health Concerns

- ☒ Cancer
- ☒ Chronic non-cancer
- ☒ Acute

Exposed Population

- ☒ Adult
- ☐ Child
- ☐ Infant

E-FAST: General Population Exposure from Industrial Releases

Sample Output

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *Incineration | *PDM Site

Site-Specific Human And Aquatic Exposures to Surface Water Releases ? Help

Chemicals ID/Re
Chem7.1

Release Activity: Manufacture Exposed Population: Adult
 Facility name: EXXON CO USA (BILLINGS REFIN.) Discharge Type: Direct
 Facility location: BILLINGSMT591031163 WWT Removal: 70.00 %
 NPDES#: MT0000477 Release days: 250.00
 Reach Number: 10070007039 Pre-treatment release: 4.00 kg/day
 Reach Name: YELLOWSTONE R Post-treatment release: 1.20 kg/day
 Facility on reach? ☒ Yes ☐ No ☐ Unk. Bio Concentration Factor: 300.00 L/kg

General Site Information | Drinking Water Information | Fish Ingestion Information

Drinking Water Exposure Estimates

Exposure Type	Results	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer					
LADDpot (mg/kg/day)	8.98E-07	30.00	75.00	71.80	1.40
LADCpot (mg/kg)	4.61E-05	30.00	75.00	NA	NA
Chronic Non-Cancer					
ADDpot (mg/kg/day)	2.25E-06	30.00	30.00	71.80	1.40
ADCpot (mg/kg)	1.15E-04	30.00	30.00	NA	NA
Acute					
ADRppt (mg/kg/day)	4.20E-05	1 day	1 day	71.80	6.00

Click on River Tab and Drinking Water Info to get Human DW Exposure Estimates

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *Incineration | *PDM Site

Site-Specific Human And Aquatic Exposures to Surface Water Releases ? Help

Chemicals ID/Re
Chem7.1

Release Activity: Manufacture Exposed Population: Adult
 Facility name: EXXON CO USA (BILLINGS REFIN.) Discharge Type: Direct
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 Reach Number: 10070007039 Pre-treatment release: 4.00 kg/day
 Reach Name: YELLOWSTONE R Post-treatment release: 1.20 kg/day
 Facility on reach? ☒ Yes ☐ No ☐ Unk. Bio Concentration Factor: 300.00 L/kg

General Site Information | Drinking Water Information | Fish Ingestion Information

Fish Ingestion Exposure Estimates

Exposure Type	Results	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer					
LADDpot (mg/kg/day)	1.15E-06	30.00	75.00	71.80	6.00
LADCpot (mg/kg)	1.38E-02	30.00	75.00	NA	NA
Chronic Non-Cancer					
ADDpot (mg/kg/day)	2.89E-06	30.00	30.00	71.80	6.00
ADCpot (mg/kg)	3.46E-02	30.00	30.00	NA	NA
Acute					
ADRppt (mg/kg/day)	9.06E-05	1 day	1 day	71.80	129.00

Click on River Tab and Fish Ingestion Info to get Human Fish Ingestion Exposure Estimates

E-FAST: General Population Exposure from Industrial Releases

Sample Output

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *Incineration | *PDM Site

Inhalation Exposure Estimates From Incineration Releases

Chemicals ID/Re
ChemZ.1

Release Activity: **Manufacture** % Removal: **99.90**

Exposed Population: **Adult** Pre-treatment release: **2.00E+05** kg/yr

Sites: **1** Post-treatment release: **200.00** kg/yr

Incineration Exposure Estimates

Exposure Type	Results	ED (yrs)	AT (yrs)	BW (kg)	IR (m3/hr)
Cancer					
LADDpot (mg/kg/day)	4.41E-08	30.00	75.00	71.80	0.55
LADCpot (mg/kg)	2.40E-07	30.00	75.00	NA	NA
Chronic Non-Cancer					
ADDpot (mg/kg/day)	1.10E-07	30.00	30.00	71.80	0.55
ADCpot (mg/kg)	6.00E-07	30.00	30.00	NA	NA

Click on Incineration Tab to get Incineration Exposure Estimates

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *Incineration | *PDM Site

Environmental Release Results

Chemicals ID/Re
ChemZ.1

Number of Sites: **1**

	Water	Landfill/Sludge	Incineration	Fugitive
Total Releases: (before treatment)	1000.00 (kg/yr)	0.00 (kg/yr)	2.00E+05 (kg/yr)	0.00 (kg/yr)
Release days/yr: (before treatment)	250.00			0.00
Per site release	4.00 (kg/site/day)	0.00 (kg/yr)	2.00E+05 (kg/yr)	0.00 (kg/site/day)

Click on Env. Rel. Tab to get Environmental Release Estimates

E-FAST: Down-the-Drain Residential Releases

What Does this Module Do?

This module estimates human and aquatic environmental exposure to chemicals released via the use and disposal of certain types of consumer products in a residential setting. This module is designed to assess releases of products that are intended to go down the drain at a home, such as liquid laundry detergent, or bathroom cleaners. Human exposures are estimated for adults, children and infants for releases to surface water. The module also estimates aquatic environmental exposure and risk from surface water releases.

This Module has built-in databases

- ❖ Human Exposure Factors;
- ❖ A generic, United States wide, consumer product use exposure scenario.

Important Note

The HELP screen contains information on model inputs, running the model, QA/QC, Calculations, and References.

Inputs

- ❖ Production Volume;
- ❖ Concentration of Concern;
- ❖ Bioconcentration Factor;
- ❖ Years in use;
- ❖ Percent Removal in Wastewater treatment.

Outputs

Human Exposure

- ❖ Drinking water exposure from surface water releases;
- ❖ Fish ingestion exposure from surface water releases;

Aquatic Environment

- ❖ Post-treatment concentration in surface water;
- ❖ Days per year the COC is exceeded;
- ❖ Percentage of the year the COC is exceeded.

Date Entry Screen

Exposure Type	50%ile Res.	10%ile Res.	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer						
LADDpot (mg/kg/day)	1.59E-07	2.06E-06	30.00	75.00	71.80	6.00
LADCpot (mg/kg)	1.90E-03	2.47E-02	30.00	75.00		
Chronic Non-Cancer						
ADDpot (mg/kg/day)	3.96E-07	5.15E-06	30.00	30.00	71.80	6.00
ADCpot (mg/kg)	4.74E-03	6.17E-02	30.00	30.00		
Acute						
ADRPot (mg/kg/day)	8.52E-06	1.11E-04	1 day	1 day	71.80	129.00

Fish Ingestion Exposure Estimates

Sample Output from E-FAST: Down-the-Drain Residential Releases

Drinking Water Exposure Estimates

E-Fast

Intro Disposal Inputs *Disposal Res.

Disposal Results ? Help

Release Activity: **Manufacture**

Production Volume: **1.12E+06** kg/year

WWT Removal: **50.00** %

Release days: **365.00** days

Bio Concentration Factor: **300.00** L/kg

Exposed Population: **Adult**

Median surface water conc: **1.58E-02** ug/L

High end surface water conc: **0.21** ug/L

Pre-treatment release: **1.13E-02** g/person/day

Post-treatment release: **5.64E-03** g/person/day

PDM Information Drinking Water Information Fish Ingestion Information

Drinking Water Exposure Estimates

Exposure Type	50%ile Res.	10%ile Res.	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer						
LADDpot (mg/kg/day)	1.23E-07	1.60E-06	30.00	75.00	71.80	1.40
LADCpot (mg/kg)	6.32E-06	8.22E-05	30.00	75.00	NA	NA
Chronic Non-Cancer						
ADDpot (mg/kg/day)	3.08E-07	4.01E-06	30.00	30.00	71.80	1.40
ADCpot (mg/kg)	1.58E-05	2.06E-04	30.00	30.00	NA	NA
Acute						
ADRppt (mg/kg/day)	1.32E-06	1.72E-05	1 day	1 day	71.80	6.00

PDM Disposal Exposure Estimates

E-Fast

Intro Disposal Inputs *Disposal Res.

Disposal Results ? Help

Release Activity: **Manufacture**

Production Volume: **1.12E+06** kg/year

WWT Removal: **50.00** %

Release days: **365.00** days

Bio Concentration Factor: **300.00** L/kg

Exposed Population: **Adult**

Median surface water conc: **1.58E-02** ug/L

High end surface water conc: **0.21** ug/L

Pre-treatment release: **1.13E-02** g/person/day

Post-treatment release: **5.64E-03** g/person/day

PDM Information Drinking Water Information Fish Ingestion Information

PDM Disposal Exposure Estimates

Concentration of concern: **10.00** ug/L

Number of days concentration of concern exceeded: **5.84** days

% of year concentration of concern exceeded: **1.60** %

E-FAST: Consumer Exposure Module (CEM)

What Does this Module Do?

This module of E-FAST estimates human inhalation and dermal exposure to chemicals in certain types of consumer products. Human exposures are estimated for adults, and where appropriate children and infants.

This Module has built-in databases

- ❖ Human exposure factors;
- ❖ Default use amounts for 9 preset scenarios;
- ❖ Activity patterns for residents in the home;
- ❖ Common chemical components of consumer products with associated “typical” weight fractions.

Important Note

The HELP screen contains information on running the modules, QA/QC, Calculations, and References.

Inhalation Exposure from the following products is predicted:

- ❖ General purpose cleaners
- ❖ Latex paint
- ❖ Fabric protector
- ❖ Aerosol paint
- ❖ Laundry detergent
- ❖ Solid air freshener
- ❖ User defined “create your own” scenario

Dermal Exposure from the following products is predicted:

- ❖ General purpose cleaners
- ❖ Latex paint
- ❖ Laundry detergent
- ❖ Bar soap
- ❖ Used motor oil
- ❖ User defined “create your own” scenario

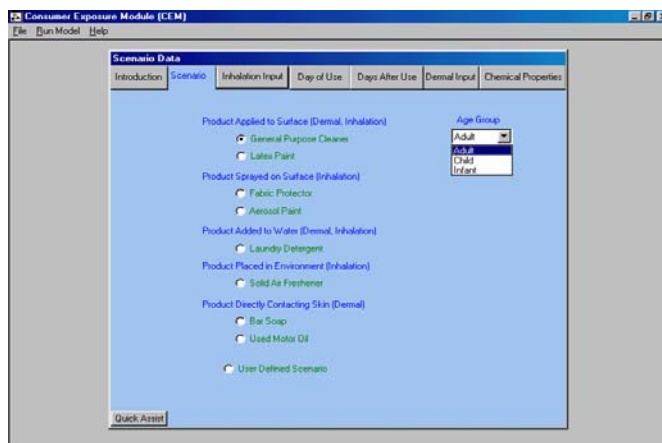
Inputs

- ❖ Weight fraction of chemical in consumer product
- ❖ Molecular weight
- ❖ Vapor pressure

Outputs

- ❖ Concentration of chemical in the indoor environment
- ❖ Inhalation exposure estimates:
 - Lifetime Average Daily Dose (LADD)
 - Average Daily Dose (ADD) and
 - Acute Potential Dose Rate (APDR)
- ❖ Dermal exposure estimates:
 - Lifetime Average Daily Dose (LADD)
 - Average Daily Dose (ADD) and
 - Acute Potential Dose Rate (APDR)

Consumer Exposure Module (CEM) Select-a-Scenario Screen



E-FAST: Consumer Exposure Module (CEM)

Consumer Exposure Module (CEM)

File Run Model Help

Introduction Scenario Inhalation Input Day of Use Days After Use Dermal Input Chemical Properties

Consumer Exposure Module (CEM)

CEM is an interactive model which calculates conservative estimates of potential inhalation and dermal exposure to consumer products. Because the model incorporates upper percentile and mean input values for various exposure factors in the calculation of potential exposures / doses, the exposure / dose estimates are considered to be 'high end' to 'bounding' estimates (Guidelines for Exposure Assessment, USEPA, 1992). The dermal portion of CEM uses a film-thickness approach, which assumes that exposure occurs from a thin layer of the consumer product on a defined surface area, to determine potential exposure. Few data exist on the actual thickness of films of various products on human skin. Therefore, due to the uncertainty associated with the amount of product forming a film on the skin, the dermal exposure estimates are considered less certain than those calculated in the inhalation portion of CEM.

Default exposure factor values have been extracted from U.S. EPA's Exposure Factors Handbook (August 1997). This handbook can be obtained from the Agency by calling (513) 569-7562, or can be obtained at the <http://www.epa.gov/ORD/WebPubs/exposure> web site.

Identification Number: Product:

Model Run Comments (this entry allows the user to enter any free flowing textual description about the model run.)

Quick Assist

Inhalation Scenario Input Screen

Consumer Exposure Module (CEM)

File Run Model Help

Introduction Scenario Inhalation Input Day of Use Days After Use Dermal Input Chemical Properties

Scenario: General Purpose Cleaner

This screen allows the user to input the required product parameters for the inhalation model.

Identification Number: Unknown Product: Unknown

Frequency of Use	<input type="text" value="804"/> events/year	Years of Use	<input type="text" value="57"/> years
Mass of Product per Event - Median	<input type="text" value="61.5"/> g	Mass of Product Used per Event - 90th %	<input type="text" value="123"/> g
Duration of Use - Median	<input type="text" value="0.667"/> hrs/ev	Duration of Use - 90th	<input type="text" value="1.42"/> hrs/ev
Air Exchange Rate	<input type="text" value="0.45"/> air xchg per hour	Body Weight	<input type="text" value="71.8"/> kg
Inhalation Rate During Use	<input type="text" value="0.55"/> m3/hr	Averaging Time - LADD, LADC	<input type="text" value="75"/> years
Inhalation Rate After Use	<input type="text" value="0.55"/> m3/hr	Averaging Time - ADD, ADC	<input type="text" value="57"/> years

Quick Assist

E-FAST: Consumer Exposure Module (CEM)

Inhalation Scenario Input Screen

Consumer Exposure Module (CEM)

File Run Model Help

Inhalation Inputs

Introduction Scenario **Inhalation Input** Day of Use Days After Use Dermal Input Chemical Properties

Scenario: General Purpose Cleaner

This screen allows the user to input the required product parameters for the inhalation model.

Identification Number: Unknown Product: Unknown

Frequency of Use: 500 events/year Years of Use: 57 years

Mass of Product Used per Event - Median: 61.5 g Mass of Product Used per Event - 90th %: 123 g

Duration of Use - Median: 0.667 hrs/ev Duration of Use - 90th: 1.42 hrs/ev

Air Exchange Rate: 0.45 air xchs per hour Body Weight: 71.8 kg

Inhalation Rate During Use: 0.55 m3/hr Averaging Time - LADD, LADC: 75 years

Inhalation Rate After Use: 0.55 m3/hr Averaging Time - ADD, ADC: 57 years

Quick Assist

Inhalation Output Screen

Consumer Exposure Module (CEM)

File Run Model Help

Inputs **Outputs - Inhalation** **Outputs - Dermal** [Return to Input Screen](#)

CEM Inhalation Exposure Estimates

ID Num: Unknown Product: Unknown

Scenario: Latex Paint Population: Adult

Inhalation Rate(m3/hr): 0.55 Years of Use(years): 11

Body Weight (kg): 71.8 Frequency of Use (events/year): 4

Exposure Units	Result	AT (days)
Chronic, Cancer		
LADD _{inh} (mg/kg-day)	3.40e-03	2.74e+04
LADC _{inh} (mg/m3)	1.90e-02	2.74e+04
Chronic Non-Cancer		
ADD _{inh} (mg/kg-day)	2.58e-02	4.02e+03
ADC _{inh} (mg/m3)	1.20e-01	4.02e+03
Acute		
ADR _{inh} (mg/kg-day)	0.05e+00	1.00e+00
Cp _{inh} (mg/m3)	1.15e-02	1.00e+00

LADD - Lifetime Average Daily Dose (mg/kg-day)
 ADD - Average Daily Dose (mg/kg-day)
 ADR - Acute Dose Rate (mg/kg-day)
 Note: 75 years = 2.73e+04 days

LADC - Lifetime Average Daily Concentration (mg/m3)
 ADC - Average Daily Concentration (mg/m3)
 Cp - Peak Concentration (mg/m3)
 AT - potential dose

Note: The general Agency guidance for assessing short-term, infrequent events (for most chemicals, an exposure of less than 24 hours that occurs no more frequently than monthly) is to treat such events as independent, acute exposures rather than as a chronic exposure. Thus, estimates of long-term average exposure like ADD or ADC may not be appropriate for use in assessing risks associated with this type of exposure pattern. (Methods for Exposure-Response Analysis for Acute Inhalation Exposures to Chemicals (External Review Draft), EPA/600/R-95/051, April 1995)

Inhalation Output Screen

Consumer Exposure Module (CEM)

File Run Model Help

Inputs **Outputs - Inhalation** **Outputs - Dermal** [Return to Input Screen](#)

ID Num: Unknown Product: Unknown

Scenario: Latex Paint Population: Adult

Years of Use (years): 11

SAW Body (m3/kg): 4.5

Frequency of Use (events/year): 4

Exposure Units	Result	AT (days)
Chronic, Cancer		
LADD _{inh} (mg/kg-day)	2.02e-03	2.74e+04
Chronic Non-Cancer		
ADD _{inh} (mg/kg-day)	1.99e-02	4.02e+03
Acute		
ADR _{inh} (mg/kg-day)	2.27e+00	1.00e+00

LADD - Lifetime Average Daily Dose (mg/kg-day)
 ADD - Average Daily Dose (mg/kg-day)
 ADR - Acute Dose Rate (mg/kg-day)
 Note: 75 years = 2.73e+04 days

AT - potential dose

Note: The general Agency guidance for assessing short-term, infrequent events (for most chemicals, an exposure of less than 24 hours that occurs no more frequently than monthly) is to treat such events as independent, acute exposures rather than as a chronic exposure. Thus, estimates of long-term average exposure like ADD or ADC may not be appropriate for use in assessing risks associated with this type of exposure pattern. (Methods for Exposure-Response Analysis for Acute Inhalation Exposures to Chemicals (External Review Draft), EPA/600/R-95/051, April 1995)

E-FAST: Consumer Exposure Module (CEM)

Dermal Input Screen

Consumer Exposure Module (CEM)

File Run Model Help

Dermal Inputs

Introduction Scenario Inhalation Input Day of Use Days After Use **Dermal Input** Chemical Properties

Scenario: General Purpose Cleaner

This screen allows the user to input the required product parameters for the dermal model.

Identification Number: Unknown Product: Unknown

Amount Retained on Skin g/cm2-event Years of Use years

Frequency of Use events/year Surface Area to Body Weight Ratio cm2/kg

Averaging Time - LADD, LADC years Averaging Time - ADD, ADC years

Quick Assist

Dermal Output Screen

Consumer Exposure Module (CEM)

File Run Model Help

Inputs **Outputs - Inhalation** **Outputs - Dermal** [Return to Input Screen](#)

CEM Inputs			
ID Num:	Unknown	Chemical Name:	ChemZ
Product:	Unknown		
Scenario:	Latex Paint	Population:	Adult
Molecular Weight (g/mole)	275	VP (torr)	0.9
WF - Med	0.1738	WF - 90 %	0.2271
Inhalation Inputs			
Frequency of Use (events/yr)	4	Years of Use	11
Mass of Product Used - Median (g)	3635	Mass of Product Used - 90 % (g)	1.272e+04
Inhalation Rate During Use (m3/hr)	0.55	Inhalation Rate After Use (m3/hr)	0.55
Zone 1 Volume (m3)	40	Whole House Volume (m3)	369
Duration of Use - Median (hrs/ev)	3	Duration of Use - 90 % (hrs/ev)	8
Air Exchange Rate (air xchg/hr)	0.45	Body Weight (kg)	71.8
Activity Patterns			
User:	1 1 1 1 1 1 1 2 3 1 1 1 1 1 1 1 1 2 7 4 4 4 1	Start Time:	10
Non-User:	1 1 1 1 1 1 1 1 3 2 4 4 2 4 7 7 4 2 2 7 4 4 4 1	Room of Use:	1. Bedroom
Hour:	0 6 12 18		
Dermal Inputs			
Frequency of Use - Body (events/yr)	4	SA/BW - Body (cm2/kg)	4.5
Amount Retained/Absorbed to Skin (g/cm2-event)	0.00232		
Averaging Time, LADD _{px} , LADC _{px}	2.74e+04	Averaging Time, ADD _{px} , ADC _{px}	4.02e+03
Averaging Time, ADR _{px} , Cp _{px}	1.00e+00		

E-FAST: Aquatic Environment Exposure / Risk

What Does this Module Do?

This module of E-FAST estimates chemical concentration in a stream and how many days per year a chemical discharged in a plant's effluent will exceed a concentration of concern in the receiving water. This module can be used with either detailed site-specific data, or more general Standard Industrial Classification (SIC) code-based information. This module can help the risk assessor estimate if the amount of chemical discharged to a stream will result in stream concentrations that may adversely affect aquatic organisms.

Inputs

Site-specific

- ❖ NPDES number
- ❖ Release days per year
- ❖ Loading - amount released after treatment (kg/day)
- ❖ CC or COC (may be estimated using ECOSAR).

SIC Code-based

- ❖ Analysis choice (usually high-end analysis)
- ❖ Standard Industrial Classification (SIC) code
- ❖ Release days per year
- ❖ Loading - amount released after treatment (kg/day)
- ❖ CC or COC

Outputs

Number of days per year the concentration in the stream will exceed the concern concentration (CC)

Input Screen

E-FAST

Intro *PDM Site *PDM SIC

Chemical ID:

PDM Site Specific Page ? Help

NPDES #: <-Find Entered NPDES Select a NPDES:

Release Activity: Discharge Type:

Facility name: WWT Removal: %

Facility location: Release days: days/yr

Reach Number: Concentration of concern: ug/L

Reach Name: Pre-treatment release: kg/day

Facility on reach? ☒ Yes ☐ No ☐ Unk. Post-treatment release: kg/day

Mean streamflow: MLD

Low streamflow: MLD

Effluent flow: MLD

PDM Site Specific Estimates

COC (ug/L)	% year exceeded	Days/year exceeded	Rel Days	Pre-treat Load	WWT
10.00	0.01	0.04	250.00	4.00	70.00

ChemSTEER – Chemical Screening Tool for Exposures and Environmental Releases

What Does ChemSTEER Do?

This personal computer-based software program generates screening-level estimates of environmental releases from and worker exposures to a chemical manufactured, processed, and/or used in industrial and commercial workplaces. The tool contains data and estimation methods and models to assess chemical use in certain common industrial/commercial sectors (e.g., automotive refinishing), as well as for certain chemical functional uses (e.g., tackifier in adhesive).

Why Use ChemSTEER?

ChemSTEER should be used when release and worker exposure data are not available but some estimates of these data are desired. ChemSTEER's methods and models are primarily intended to assess some primary sources of workplace releases and activities with worker exposure potential that are specific to a particular industry (e.g., overspray from auto body refinishing) and other sources of workplace releases and activities with worker exposure potential that are "broadly applicable" across many workplaces (e.g., drumming semi-volatile liquid, scooping/ weighing small volumes of powders, etc.). The "broadly applicable" sources/ activities available in ChemSTEER are only a subset of all possible sources and activities and primarily cover those sources/ activities that are often overlooked or considered to be non-routine or insignificant.

What You Need To Use ChemSTEER

- ❖ Understanding of the 27 models and associated methods (mass balance & container-related calculations) in ChemSTEER can make your use of the tool most effective and help you to know which data inputs you need for an assessment;
- ❖ Understanding of the operations (i.e., workplaces) to be assessed)except for industry- sector uses included in ChemSTEER).

Inputs

Required inputs depend upon the model(s) you intend to use.

Chemical-specific inputs that are helpful or needed:

- ❖ Production volume (domestic, imported, and total);
- ❖ Vapor pressure and Molecular weight (when the assessed chemical is semi-volatile or volatile);
- ❖ Density; and
- ❖ Solubility in water.

Operation-specific inputs that are helpful or needed:

- ❖ Understanding of what operations (workplaces) are to be assessed; knowledge of the relationships between multiple operations being assessed;
- ❖ Knowledge of the sources of release and/or worker exposure activities contained within each operation (not as important for industry- sector uses included in ChemSTEER);
- ❖ Certain operating information and parameters (e.g., throughput volumes, physical state(s) and concentration(s) of the chemical or the mixture(s) containing the chemical in the operation, number of sites, number of operating days per year, number of batches run per year, number of workers per site, container types and sizes, etc.) (not as important for industry- sector uses included in ChemSTEER).

ChemSTEER uses default values for many parameters in the absence of user inputs; however, users who become familiar with the models used to calculate chemical releases to the environment and worker exposures to the chemical can use those models most effectively. The ChemSTEER Help System contains detailed descriptions of each estimation model and input parameter.

The following pages cover the most important data entry for ChemSTEER. Many fields that are not covered are primarily for recordkeeping and thought processes meant to improve the assessment.

ChemSTEER – Chemical Input Screen

P02-9998

File Edit Reports Help

General **Chemical** Operations Operation Parameters Releases Exposures Optional Information

Chemical

Chemical Name: Toluene

Chemical Category:

Trade Name(s):

Chemical CAS Number: 108-88-3 Molecular Formula: C7H8

Total Assessed Production Volume (PV): 11200 kg/yr Type of Notice:

Imported Production Volume (PVI): 1200 kg/yr

Domestic Production Volume (PVD): 10000 kg/yr

Vapor Pressure (VPchem): 0.029 torr at 20 C

Molecular Weight (MW): 92 g/mol % < 500: % < 1000:

Density (Dchem): 0.87 g/cm3 at C

Solubility in Water (WSchem): 53 g/L at C

General Description of End Use(s): solvent used in coatings

View/Update Exposure Limits Update Chemical Information View/Update Regulatory Limits

Parameters with red labeling are often important defaults used in mass balance, container, and model calculations.

What is the Chemical tab used for?

You can view and/or enter information about the chemical to be assessed on the Chemical tab. The fields shown in red font are for parameters commonly used by EPA in completing assessments. Volume parameters are used extensively in generating release- and exposure-related estimates. Volume parameters include import and domestic production volumes (or volumes to be assessed). Chemical property parameters are commonly used in some of the ChemSTEER methods and models.

How is the chemical's production volume (PV) important to the assessment?

The PV entered in this screen is used by virtually all of the ChemSTEER algorithms to determine output values for the assessment, such as:

- ❖ Number of sites manufacturing or using the chemical;
- ❖ Number of operating days at the sites; and
- ❖ Amount of the chemical released to the environment.

How are the chemical's vapor pressure, molecular weight, and density important to the assessment?

- ❖ Vapor pressure and molecular weight are used by several release and inhalation exposure models to estimate the amount of volatile chemical released, as well as the amount of chemical vapor that is inhaled by workers.
- ❖ Density is used to determine numbers of containers that may be filled with the chemical and/or emptied at each site – which in turn is used to estimate amounts of residual container waste and duration of worker exposures.

Users are encouraged to review the ChemSTEER Help System topics that discuss the estimation model calculations and associated input parameters.

ChemSTEER – Sample Operation Input Screen

ChemSTEER 10/31/2002 Version - P02-9998

File Edit Reports Help

General Chemical Operations Operation Parameters Releases Exposures Optional Information

Operations
Select an operation below to see its Description; the Physical State(s) of the chemical; Relationships to other operations; Sources and Activities associated with Release and Exposures; and Site Information.

Manufacture
Formulation of paint product
Formulation of cleaner
Automobile OEM Spray Coating

Update Operations

Description Relationships Physical States Sources/Activities Site Information

Sources and Activities associated with releases and exposures within the operation:

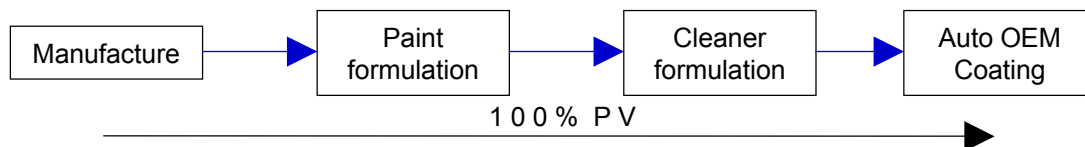
Activity	Release	Exposure
Unloading Liquid Raw Material from Drums	Yes	Yes
Cleaning Liquid Residuals from Drums Used to Transport the Raw Material	Yes	Yes
Equipment Cleaning Losses of Liquids from a Single, Large Vessel	Yes	No
Loading Liquid Product into Bottles	Yes	Yes

Update Sources/Activities

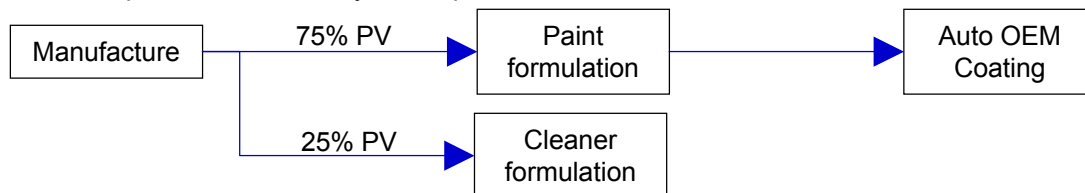
What is the Operation tab used for?

You can use this screen to “build” the structure of the assessment. You must select one or more **operations (workplaces)** in which the chemical is manufactured, processed, and/or used - see top list in the screen) to assess. Then you should complete at least the two primary subtabs as follows:

❖ Relationships subtab: For partial or full lifecycle assessments, you should define the relationship between the operations (2nd subtab). For example, in the assessment shown above, the user was able to change the operation relationship from the default of a straight series lifecycle of operations:



to a more complex, branched lifecycle of operations:



❖ Sources/ Activities subtab: For each operation, you must select the release sources and worker activities (i.e., **sources/ activities** - see bottom list in the screen) to assess. In the example shown above, there are four sources/activities included in the “Formulation of paint” operation. This selection is critical because it determines which default models are used to estimate releases and exposures.

ChemSTEER – Operation Parameter Input Screen

ChemSTEER 10/31/2002 Version - P02-9998

File Edit Reports Help

General Chemical Operations **Operation Parameters** Releases Exposures Optional Information

Operation Parameters

Manufacture
Formulation of paint product
Formulation of cleaner
Automobile OEM Spray Coating

Mass Balance Parameters Container Parameters

Parameter	Type	Value
BMlchem: Batch Mass Input of Chemical	User Specified	10
BMOchem: Batch Mass Output of Chemical	Default/Derived	10
BMlrm: Batch Mass Input of Raw Material	Default/Derived	11.1111
BMOprod: Batch Mass Output of Product	User Specified	100
NS: Number of Sites	User Specified	5
Nby: Number of Batches per Year	Default/Derived	168
Yrm: Weight Fraction of Chemical in Raw Material	User Specified	0.9
Yprod: Weight Fraction of Chemical in Product	User Specified	0.1
HB: Hours per batch	User Specified	24
ODmax: Maximum number of operating days	User Specified	365
Nbld: Number of batches per line per day	Default/Derived	1.0
Ls: Lines per site	Default/Derived	1
OD: Number of Operating Days	Default/Derived	168
Nbd: Number of Batches per Day	Default/Derived	1

Update Parameters

What is the Operation Parameters screen used for?

Many of the parameters entered or calculated in this screen are used in determining input values to models. Knowledgeable users can discern when one or both of these sections can be left incomplete (e.g., in some simple or partial assessments, models can be used without completing these sections).

What are operation mass balance parameters?

The operation mass balance parameters are the set of input values that define the operation and associated chemical throughputs (see above for a list of operation mass balance parameters). The user may choose several options for calculating the operation mass balance parameters, based on what values are known and which must be calculated. Some examples are listed below:

- ❖ Are the influent or effluent parameters known?
- ❖ Is the use rate of the chemical known? Is the production rate of the product known?
- ❖ Are the number of sites and operating days per year known?

Industry- sector uses included in ChemSTEER contain default values for mass balance parameters.

What are operation container parameters?

Container parameters are the set of input values that define the number of containers that are filled with the chemical and/or emptied during the operation. These values are most often used to estimate amounts of residual container waste and duration of worker exposures during loading and unloading activities. Handling of shipping containers are often overlooked as release sources/ exposure activities.

The ChemSTEER Help System contains an extensive description of how the mass balance and container parameters are calculated and subsequently used by various release and exposure estimation models. Users are encouraged to take time to learn about these complex functions.

ChemSTEER – Release Input Parameters Subtab

Estimating Chemical Releases

All activities that have a chemical release are listed below. Each has one or more release estimation models associated with it. When a release activity is selected, one or more release models will be shown in the Release Model(s) list. Select each model in the Release Model(s) for Selected Activity list to view parameters for the model, and click the View/ Update Model Information button to view model equations and to change parameter values.

Operation:

Release Activity:

Release Model(s) for Selected Activity:

Release Input Parameters | Estimated Releases

Parameter	Type	Value Calc	Value	Units
f: Saturation Factor	Default	Model Parm	1	dimensionless
Freq: Frequency to Use	Default	QDa	168	days/yr
G: Vapor Generation Rate	Model Output	Model Parm	9.058116E-06	g/s
MW: Molecular Weight	Default	Chem Parm	92	daltons
NS: Number of Sites	Default	Mass Parm	5	sites
Oh: Operating Hours for the Activity	Default	Cont Parm	0.5061318	hours/day
r: Container Rate	Default	Cont Parm	60	containers/hr
R: Universal Gas Constant	Constant	Model Parm	82.05	atm cm ³ /gmol K
T: Temperature	Default	Model Parm	298	K
Vc: Volume Capacity of container	Default	Cont Parm	1	gal/container
VP: Vapor Pressure	Default	Chem Parm	0.029	torr
X: Vapor Pressure Correction Factor	Default	Model Parm	1	dimensionless

Add or Remove a Release model

View/Update Model Information

Modify Media of Release

View/Update Combinations

Run Model(s)

What are the Release and Exposure screens used for?

Based on the information input on the Chemical, Operation, and Operation Parameters screens, ChemSTEER chooses the default model appropriate to each source/ activity for each operation. The Release and Exposure screens display the model selected for the operation and sources/ activity shown in the selection lists on those screens. These screens also display model inputs and outputs, and give the user the ability to change models and default values used in models.

For each source/activity, there is at least one default release and/or worker exposure model that are used to estimate the chemical releases and/or worker exposures that occur during the activity. The user may select an alternative model to the default.

For some sources/ activities on the Release screen, more than one release model may be appropriate (e.g., a vapor generation model and a residual model).

However, for each source/ activity on the Exposure screen, a maximum of one model may be selected for each route of worker exposure (inhalation and/ or dermal) assessed.

You can view input parameters to the models and model outputs in the view lists at the bottom of these screens (the example above shows the inputs list for a release model).

You can use the buttons on these screens to:

- ❖ Change models;
- ❖ View model equations and change model parameters;
- ❖ Change release medium or media (for releases only); and
- ❖ Run models.

ChemSTEER – Example Release Model Parameters Input Screen

View / Update Release Model Information

Read-only and updatable information about the selected release model, including the model equation, mechanism, basis, and input parameters are listed below. Because the release can be calculated using several valid equations for this model, all of the possible parameters that may be used are listed in the Input Parameters grid. Depending on the data values for this release, some of these parameters will not be required. To view options or change a parameter value, click on the label for that parameter under the Type column. When Type is User-defined, you must click on the cell under the value column and type in your own value.

Activity: Loading Liquid Product into Bottles
 Model: EPA/OAQPS AP-42 Loading Model

Model Equation: $DR \text{ (kg/site-day)} = (G \times 3600 \times OHa) / 1000$
 $DR \text{ occurs over [Freq] days/year}$

Mechanism: Displacement of air containing chemical vapor

Basis: EPA/OAQPS AP-42 Loading Model

Parameter	Type	Value Calc	Value	Units
OHa: Operating Hours for the Activity	Default	Cont Parm	0.5061318	hours/day
r: Container Rate	Default	Cont Parm	60	containers/hr
R: Universal Gas Constant	Constant	Model Parm	82.05	atm cm ³ /gmol K
T: Temperature	Default	Model Parm	298	K
Vc: Volume Capacity of container	Default	Cont Parm	1	gal/container
VP: Vapor Pressure	Default	Chem Parm	0.029	torr

OK Cancel

ChemSTEER Release and Exposure Models

Each release and exposure model contains the necessary input parameter values to perform the calculation – these values are either determined from input from a previous input screen or have been assigned a default value.

In the example screen shown above accessed from the View/ Update Model Information button on the Release tab, the input parameters' values (listed in the lower portion of the screen) were determined as follows:

- ❖ OHa (Operating hours for the activity) – entered or calculated in the Container Parameters Input Screen
- ❖ r (Container rate – containers filled per hour) – entered or calculated in the Container Parameters Input Screen
- ❖ R (Universal Gas Constant) – default value assigned by the model
- ❖ T (Temperature) – default value assigned by the model
- ❖ Vc (Volume capacity of each container) – entered or calculated in the Container Parameters Input screen
- ❖ VP (Vapor pressure) – entered in the Chemical Input screen

The user may elect to modify any of the model input parameters that are NOT determined through calculations performed in other input screens; however, users are strongly encouraged to review the associated ChemSTEER Help System topic before modifying the default model input parameters.

This screen also shows the model equation(s) that use the input parameters listed.

ChemSTEER – Sample Release Output Screen

Outputs

Environmental Release:

- ❖ Media of release (e.g., air, water, incineration, and/or landfill)
- ❖ Number of sites releasing the chemical to the environment
- ❖ Daily release rate (kg chemical per site-year)
- ❖ Days of release (days per site-year)
- ❖ Annual release rate (kg chemical per year)

ChemSTEER 10/31/2002 Version - P02-9998

File Edit Reports Help

General Chemical Operations Operation Parameters Releases Exposures Optional Information

Estimating Chemical Releases

All activities that have a chemical release are listed below. Each has one or more release estimation models associated with it. When a release activity is selected, one or more release models will be shown in the Release Model(s) list. Select each model in the Release Model(s) for Selected Activity list to view parameters for the model, and click the View/ Update Model Information button to view model equations and to change parameter values.

Operation: Formulation of paint product

Release Activity: Loading Liquid Product into Bottles

Release Model(s) for Selected Activity:

EPA/DAQPS AP-42 Loading Model

Release Input Parameters Estimated Releases

Media	Number of Sites	Daily Release Rate (kg/site-day)	Annual Release Rate (kg/yr-all sites)	Days of Release (days/site-yr)	Basis
Air	5	1.6505E-05	0.014	168	EPA/DAQPS

Add or Remove a Release model

View/Update Model Information

Modify Media of Release

View/Update Combinations

Run Model(s)

ChemSTEER – Example Exposure Output Screen

Outputs (Continued)

Worker Exposures (Inhalation and Dermal):

- ❖ Potential dose rate (mg per day)
- ❖ Lifetime average daily dose (mg per kg-day)
- ❖ Average daily dose (mg per kg-day)
- ❖ Acute potential dose (mg per kg-day)

ChemSTEER 10/31/2002 Version - P02-9998

File Edit Reports Help

General Chemical Operations Operation Parameters Releases **Exposures** Optional Information

Estimating Chemical Exposures

All activities that have a chemical exposure are listed below. Each has one or more exposure estimation models associated with it. When an exposure activity is selected, one or more exposure models will be shown in the Exposure Model(s) list. Click on either the Dermal or Inhalation Input Parameters tab below to view parameters for the model, and click the View/ Update Model Information button to view model equations and to change parameter values.

Operation: Formulation of paint product

Exposure Activity: Loading Liquid Product into Bottles

Dermal Exposure Model: EPA/OPPT 2-Hand Dermal Contact with Liquid Model Liquid

Inhalation Exposure Model: EPA/OPPT Mass Balance Model Vapor

Dermal Model Input Parameters Inhalation Model Input Parameters **Activity Exposure Estimates**

Exposure	Estimate	Units
Inhalation Potential Dose Rate	3.7537	mg/day
Inhalation Lifetime Average Daily Dose	0.014	mg/kg-day
Inhalation Average Daily Dose	0.025	mg/kg-day
Inhalation Acute Potential Dose	0.054	mg/kg-day
Dermal Exposure Dose Rate	176.4	mg/day
Dermal Lifetime Average Daily Dose	0.6628	mg/kg-day
Dermal Average Daily Dose	1.1599	mg/kg-day
Dermal Acute Potential Dose	2.52	mg/kg-day

Add or Remove an Exposure model

View/Update Model Information

View/Update Combinations

Run Model(s)

Saving and Opening Your Assessments

Assessments may be saved as individual records in a database file containing multiple records or as their own individual database files.

If you open an Assessment (record) from an existing database file, you may view and/or edit the assessment on the ChemSTEER interfaces (screen views).

You may choose File/ Save Assessment to overwrite the Assessment that is in the existing database file with the working assessment that is displayed on the ChemSTEER interfaces.

If the existing database file contains more than one Assessment record, a table of Assessment records will appear that includes four fields in the record: Type, Identifier, Status, and Date. These fields must be completed on the General screen (the first screen that appears after running ChemSTEER).

You should review the ChemSTEER Help topics under the Guide to ChemSTEER Menus (File) to learn more about saving and opening assessments.

ChemSTEER – Sample EPA Report Output

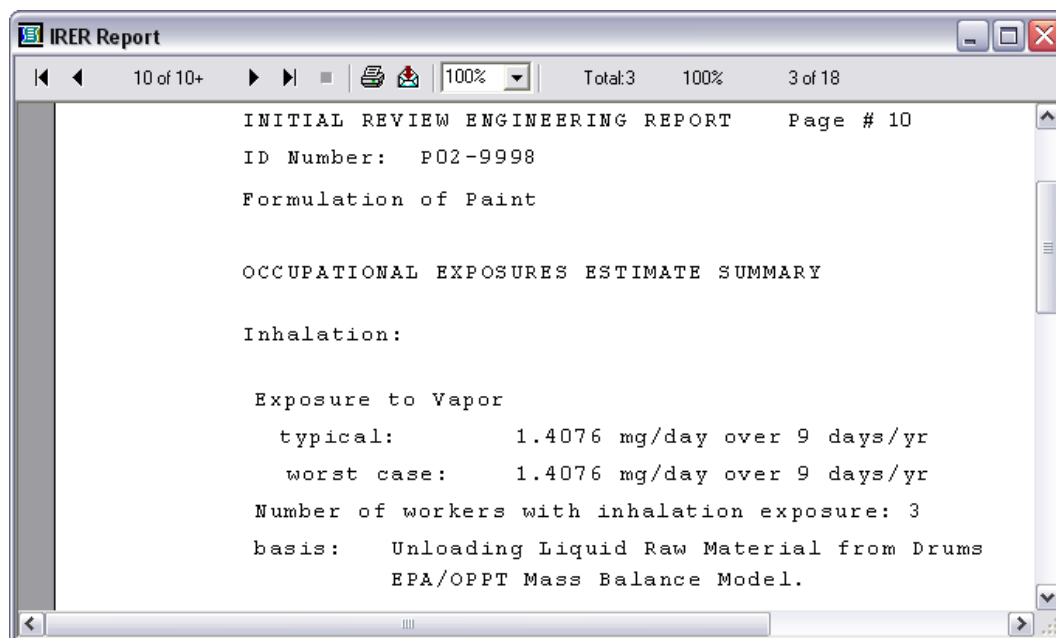
Reports

Users may view and print or export a copy of the EPA-formatted Initial Review Engineering Report (IRER) or Contact Report from the working assessment. You should review the ChemSTEER Help topics under the Guide to ChemSTEER Menus (Reports) to learn more about these options.

- ❖ The **Contact Report** summarizes the information obtained via an external contact.
- ❖ The **IRER** (shown below) is a specially formatted internal-EPA report for summarizing estimates of workplace releases and exposures in a particular assessment.

These two types of reports will appear in view windows from which you may print the report. You may also export the report into various types of file formats (e.g., rich text format) to a choice of destinations (e.g., disk).

Future versions of ChemSTEER will have additional report formats available.



Does ChemSTEER have any built-in databases?

ChemSTEER contains the list of NAICS (North American Industry Classification System) codes with descriptions that can be associated with an operation.

In a future version of the software, ChemSTEER will contain a database of the OSHA permissible exposure limits (PELs) and NIOSH recommended exposure limits (RELs) that the user can incorporate into several of the exposure model calculations.

SIC Codes for 40 Industries

#	INDUSTRY	Standard Industrial Classification (SIC) Code(s)
1	Adhesives and Sealants Manufacture	2891
2	Auto and Other Laundries	7211, 7213-7219, 7542
3	Can (metal) Manufacture	3411
4	Dyes and Pigments Manufacture	2865
5	Electronic Components Manufacture	3674, 3679
6	Electroplating	3471
7	Foundries	332, 336
8	Ink Formulation	2983
9	Inorganic Chemicals Manufacture	281
10	Large Household Appliances and Parts Manufacture	3631-3633, 3639, 3431, 3469
11	Leather Tanning and Finishing	3111
12	Lubricant Manufacture	2911, 2992
13	Manufacture of Photographic Equipment and Supplies, Photographic Processing	7221, 7333, 7395, 7819
14	Metal Finishing	3411-62, 3465-71, 3482-3599, 3613-23, 3629, 3634-6, 3643-51, 3661-71, 3673, 3676-8, 3693-4, 3699, 3711-3841, 3851, 3873-999
15	Motor Vehicle Manufacture	3711, 3713
16	Organic Chemicals Manufacture	2865, 2869
17	Ore Mining and Dressing	101-109
18	Paint Formulation	2851
19	Paper and Paperboard Mills	2621, 2631, 2661
20	Paper Mills except Building Paper Mills	2621
21	Paper Board Mills	2631
22	Building Paper and Board Mills	2661
23	Pesticides Manufacture	2819, 2869, 2879
24	Petroleum Refining	2911
25	Plastic Products Manufacture	3079
26	Plastic Resins and Synthetic Fabrics	2821, 2823, 2824
27	POTWs (Industrial)	4952
28	POTWs (All Facilities)	4952
29	Primary Metal Forming Manufacture	3315-17, 3351-57, 3463, 3497
30	Printing	271-277
31	Pulp Mills	2611
32	Rubber Products Manufacture	3011, 3021, 3031, 3041
33	Soaps, Detergents, etc. Manufacture	2841-44
34	Steam Electric Power Plants	4911
35	Textile Dyeing and Finishing (Carpets)	2271-72, 2279
36	Textile Dyeing and Finishing (Knit Goods)	225, 2292
37	Textile Dyeing and Finishing (Wool Goods)	2231
38	Textile Dyeing and Finishing (Woven Goods)	2261-62, 2269
39	Textile Dyeing and Finishing (Knit, Wool, and Woven Goods)	2231, 2250, 2269, 2292
40	Yarn and Thread Mills	2281-84

Glossary of Useful Terms

7Q10 flow: Lowest 7-consecutive day average stream flow over a 10 year period (used to assess chronic risks to aquatic life).

Acute toxicity: Adverse effects on any living organism that results from a single dose or single exposure of a chemical; any poisonous effect produced within a short period of time, usually less than 96 hours.

ADD (Average daily dose): The estimate of dose averaged over the number of years of use/exposure to the chemical; used in assessments of risk of non-cancer chronic health effects.

APDR (Acute potential dose rate): The estimated dose on a given day; used in assessments of the risk of acute toxic effects.

BCF: Bioconcentration factor (BCF) is the ratio (in L/kg) of a chemical's concentration in the tissue of an aquatic organism to its concentration in the ambient water. BCF indicates the potential for the chemical to concentrate in lipids (fats) of organisms.

Bioaccumulation: Process in which lipid soluble chemicals are stored in fatty tissue (lipids) of organisms and can increase in concentration over time.

Bioassay: Testing method that measures the effects of a material on living organisms.

Bioconcentration: Bioaccumulation of lipid soluble chemicals in fatty tissues (lipids) of organisms at concentrations higher than that of the surrounding water.

Biodegradable: Ability of a substance to be broken down physically and/or chemically by microorganisms.

Biomagnification: Process in which lipid soluble substances increase in fatty tissues (lipids) of organisms higher in the food web as contaminated food species are consumed.

Carcinogen(ic): Ability of a substance to cause cancer.

Chemical Abstract Service (CAS): Organization which assigns unique numbers to chemical substances submitted to them. CAS Registry Numbers are the unique identifier for a chemical substance, while chemical names may not be unique.

Chemical class: The general chemical group to which a chemical belongs (e.g., acid, base, hydrocarbon, etc.).

Chronic Toxicity: Adverse effects on any living organism in which symptoms develop slowly over a period of time (often the life time of the organism) or reoccur frequently.

Concern concentration (CC) or Concentration of Concern (COC): Reported in parts per billion (ppb) or parts per million (ppm), provides the concentration of a chemical in a stream and indicates the concentration at which harm is more likely to occur to aquatic organisms. CC is determined by dividing the lowest chronic toxicity value by 10.

Direct discharge: Under NPDES permitting, the discharge of chemicals or compounds directly to a surface water body.

Dose: In terms of monitoring exposure levels, the amount of a toxic substance taken into the body over a given period of time.

Dose Response: The manner in which an organism's response to a toxic substance changes as its overall exposure to the substance changes.

EC50 (Effective Concentration 50): Median effective concentration is the concentration of a pollutant at which 50% of the test organisms die; a common measure of acute toxicity.

Glossary of Useful Terms (continued)

Effluent: The stream flowing out of a facility or water body. The concentrations in it's flow are used to estimate potential health effects of the discharge.

Exposure: Pollutants that come in contact with the body and present a potential health threat, via inhalation, ingestion, or dermal routes. The route, magnitude, and duration of exposure contributes to the ultimate risk for the organism.

Half-life: Time required for one-half of a chemical or compound to degrade.

Harmonic mean: The number of daily flow measurements divided by the sum of the reciprocals of the flows. A value that is more conservative than the arithmetic mean flow value. Used to assess chronic risks to humans.

Hazard: Potential for a substance to cause adverse effects to organisms, for example birth defects.

High end: A plausible estimate of an individual exposure or dose for those persons at the upper end of an exposure or dose distribution, above the 90th percentile, but no higher than the individual in the population who has the highest exposure.

Hydrophilic: Having an affinity for, or capable of dissolving in, water.

Influent: Stream flowing into a facility or water body.

Indirect discharge: Under NPDES permitting, unlike a direct discharger, an indirect discharger from a nonresidential source pumps effluent to another facility that has a permit to discharge to the stream. Indirect dischargers often pretreat their discharges prior to pumping them to the publicly owned treatment works.

KOC: Organic carbon partition coefficient - the ratio of amount of a chemical adsorbed per unit weight of organic carbon to the chemical concentration in solution at equilibrium. Is an indication of how the chemical will partition itself between the solid and solution phases of a water-saturated or unsaturated soil.

KOW: Octanol-water partition coefficient - the ratio of a chemical's concentration in the octanol phase to it's concentration in the aqueous phase of a two-phase octanol/water system.

LADD (Lifetime average daily dose): The estimated dose to an individual averaged over a lifetime of 70 years; used in assessments of *carcinogenic* risk.

LC50 (Lethal Concentration 50): Median lethal concentration is the concentration of a pollutant at which 50% of the test organisms die; a common measure of acute toxicity.

LD50 (Lethal Dose 50): The dose of a toxicant that will kill 50% of test organisms within a designated period of time. The lower the LD50, the more toxic the compound.

Lipophilic: Having an affinity for, or capable of dissolving in, fat and fatty materials.

Loading: The amount of chemical that is discharged to a stream after treatment, reported in kg/day.

Milligrams/liter (mg/L): A measure of concentration used in the measurement of fluids that is roughly equivalent to parts per million.

Moiety(ies): Compounds formed when a larger compound is subdivided.

MSDS (Material Safety Data Sheet): Printed material concerning a hazardous chemical including its physical properties, hazards to personnel, fire and explosive potential safe handling and transportation recommendations, health effects, reactivity, and proper disposal. Originally established for employee safety by OSHA.

Mutagenicity: The property of a chemical to cause genetic mutations that are expressed in the next generation but not necessarily in the organism exposed to the mutagen.

Glossary of Useful Terms (continued)

No Observed Adverse Effect Level (NOAEL) or No Observed Effect Level (NOEL): Level of exposure which does not cause observable harm.

NPDES (National Pollutant Discharge Elimination System): is the primary permitting program under the Clean Water Act which requires that dischargers of chemicals to surface waters obtain a permit from EPA. A NPDES permit number is a nine-character number with the two letter State abbreviation beginning the number (e.g., NC0001234).

Parts per billion (ppb): One ppb is comparable to one kernel of corn in a filled, 45-foot silo, 16 feet in diameter.

Parts per million(ppm): One ppm is comparable to one drop in the gasoline tank of a full-size car.

Parts per trillion (ppt): One ppt is comparable to one drop in a swimming pool the size of a football field and 43 feet deep.

Permissible Exposure Limit (PEL): Workplace exposure limits for contaminants established by OSHA.

Point Source: A stationary location or fixed facility such as an industry or municipality that discharges pollutants into air or surface water.

Pollution: Any substances in environmental media that degrade the natural quality of the environment.

Pollution Prevention (P2): The concept stating that it is easier to prevent pollution than to clean up pollution after it has occurred.

Potential Dose Rate(s) PDR(s): Provide an estimate of possible exposure rate to receptor from expected use, usually derived by modeling using default exposure factors.

POTW (Publicly Owned Treatment Works): A municipal or public service district sewage treatment system.

Reach: A reach is a stream or river segment identified by EPA and assigned an 11-digit ID number. The first two numbers indicate the hydrologic region of the United States in which the reach is located.

Reference Dose (RfD): The concentration of a chemical that is known to cause health problems.

Release: Any spilling, leaking, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, or disposing into the environment of a hazardous or toxic chemical.

Risk: A measure of the chance that damage to life, health, property, or the environment will occur.

Risk Assessment: A process to determine the increased risk from exposure to environmental pollutants together with an estimate of the severity of impact. Risk assessments use specific chemical information plus risk factors.

SARs: Structure Activity Relationship (SAR) predict the toxicity of chemicals based on their structural similarity to chemicals for which toxicity data are available. SARs express the correlations between a compound's physicochemical properties and its toxicity. SARs measured for one compound can be used to predict the toxicity of similar compounds belonging to the same chemical class. EPA routinely uses to estimate toxicity of chemicals submitted as Pre-Manufacture Notices mandated by Section 5 of the Toxic Substances Control Act (TSCA).

SIC Code: Standard Industrial Classification Code system is a four digit number that identifies the specific industrial activity. For a complete listing of SIC codes, see Standard Industrial Classification Manual. 1987. Supt. of Documents, U.S. Government Printing Office, Washington, DC.

Toxicity Testing: Biological testing (usually with an invertebrate, fish, or small mammal) to determine the adverse effects, if any, of a chemical substance.

APPENDIX A

Case Studies

Case Study A - Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Uses the Models ECOSAR and the E-FAST General Population Exposure from Industrial Releases Module

Case Study B - Consumer Dermal Exposure

Uses the E-FAST Consumer Exposure Pathway (CEM) Module

Case Study C – Workplace Releases and Exposures

Uses ChemSTEER - the Chemical Screening Tool for Exposures and Environmental Releases

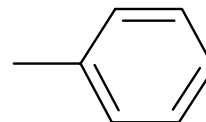
CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Introduction

The purpose of this case study is to determine the aquatic toxicity of Chemical A and to assess potential aquatic impacts and human exposures that may occur as a result of *effluent* discharges from the manufacturing facility (Company ABCDE) in Smalltown, New York. The following models will be used to accomplish this task: ECOSAR and E-FAST: General Population Exposure from Industrial Releases module.

- ECOSAR will be used first to estimate a *concern concentration* for the chemical.
- E-FAST will then be used to estimate the surface water concentration and the likelihood of potential impacts.

Chemical A (structure at right) is a compound in the neutral organic chemical class. No significant aquatic toxicity testing has been done on Chemical A.



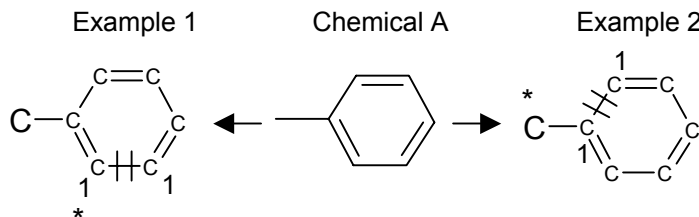
Step 1. Toxicity Determination

Because no aquatic toxicity data are available for Chemical A, ECOSAR will be used to predict its aquatic toxicity based on structural similarities to other neutral organic chemicals. The following physical/chemical properties will be assumed for Chemical A that are inputs to run the ECOSAR and E-FAST models:

- measured water solubility = 573.1 mg/L;
- melting point = 25° C;
- log *KOW* = 2.540 (ClogP);
- measured log *KOW* = 2.730; and
- fish *BCF* = 175 (not log *BCF*).

Running ECOSAR

Since you have no *CAS Number* for Chemical A, you will need to write SMILES notation to run ECOSAR. For help in writing SMILES see Appendix C or the Help screen in ECOSAR. There are many correct ways to write SMILES for a given chemical. Two examples are given below. Start the SMILES string at the “*”.



Example 1 SMILES = c1c(C)cccc1

Example 2 SMILES = Cc1ccccc1

Open ECOSAR and select “All Others” Chemicals group. Enter measured data and SMILES notation (Figure A1), then click on Calculate button. Figure A2 presents the results of running the model.

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Figure A1
ECOSAR Data Entry Screen

Ecosar v0.99g

File Edit Functions BatchMode ShowStructure Special_Classes Help

Previous Get User Save User CAS Input Calculate

Enter SMILES:

Enter NAME:

CAS Number:

Chemical ID 1:

Chemical ID 2:

Chemical ID 3:

Measured Water Sol (mg/L):

Melting Point (deg C):

Log Kow:

Measured Log Kow:

SMILES : c(cccc1)(c1)C
 CHEM : Benzene, methyl-
 CAS Num: 000108-88-3
 ChemID1:
 ChemID2:
 ChemID3:
 MOL FOR: C7 H8
 MOL WT : 92.14
 Log Kow: 2.54 (User entered)
 Melt Pt: 25.00 deg C
 Wat Sol: 573.1 mg/L (measured)

ECOSAR v0.99g Class(es) Found

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organics				
Neutral Organic SAR (Baseline Toxicity)	: Fish	14-day	LC50	41.891
Neutral Organics	: Fish	96-hr	LC50	21.225
Neutral Organics	: Fish	14-day	LC50	41.891
Neutral Organics	: Daphnid	48-hr	LC50	23.608
Neutral Organics	: Green Algae	96-hr	EC50	15.225
Neutral Organics	: Fish	30-day	ChV	2.983
Neutral Organics	: Daphnid	16-day	EC50	1.533
Neutral Organics	: Green Algae	96-hr	ChV	2.080
Neutral Organics	: Fish (SW)	96-hr	LC50	6.313
Neutral Organics	: Mysid Shrimp	96-hr	LC50	4.163
				mg/kg (ppm) dry wt soil
Neutral Organics	: Earthworm	14-day	LC50	386.488

Note* = asterick designates: Chemical may not be soluble enough to measure this predicted effect.
 Fish and daphnid acute toxicity log Kow cutoff: 5.0
 Green algal EC50 toxicity log Kow cutoff: 6.4
 Chronic toxicity log Kow cutoff: 8.0
 MW cutoff: 1000

Inputs:

❖ SMILES

❖ Chemical Name

❖ Data

Log Kow (ClogP) 2.540
 Meas. WS 573.1
 Meas. MP 25.0
 Meas. Log Kow 2.730

Figure A2
Results of Running
ECOSAR

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Figure A2
Results of Running ECOSAR

Inputs: SMILES Chemical Name Log Kow (ClogP) 2.540 Meas. WS 573.1 Melting Pt 25.0 Meas. Log Kow 2.730				
SMILES : c(cccc1)(c1)C CHEM : Benzene, methyl- CAS Num: 000108-88-3 ChemID1: ChemID2: ChemID3: MOL FOR: C7 H8 MOL WT : 92.14 Log Kow: 2.54 (User entered) Melt Pt: 25.00 deg C Wat Sol: 573.1 mg/L (measured)				
ECOSAR v0.99g Class(es) Found Neutral Organics				
ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
=====	=====	=====	=====	=====
Neutral Organic SAR (Baseline Toxicity)	: Fish	14-day	LC50	41.891
Neutral Organics	: Fish	96-hr	LC50	21.225
Neutral Organics	: Fish	14-day	LC50	41.891
Neutral Organics	: Daphnid	48-hr	LC50	23.608
Neutral Organics	: Green Algae	96-hr	EC50	15.225
Neutral Organics	: Fish	30-day	ChV	2.983
Neutral Organics	: Daphnid	16-day	EC50	1.533
Neutral Organics	: Green Algae	96-hr	ChV	2.080
Neutral Organics	: Fish (SW)	96-hr	LC50	6.313
Neutral Organics	: Mysid Shrimp	96-hr	LC50	4.163
				mg/kg (ppm) dry wt soil
				=====
Neutral Organics	: Earthworm	14-day	LC50	386.488
Note* = asterick designates: Chemical may not be soluble enough to measure this predicted effect. Fish and daphnid acute toxicity log Kow cutoff: 5.0 Green algal EC50 toxicity log Kow cutoff: 6.4 Chronic toxicity log Kow cutoff: 8.0 MW cutoff: 1000				

Note: The standard toxicity profile used by EPA for freshwater species is:

Acute Effects:	Fish	96-hr LC50 (mg/L)
	Daphnid	48-hr LC50
	Green algal	96-hr EC50
Chronic Effects:	Fish	ChV
	Daphnid	ChV or 16d EC50
	Green algal	ChV

Chemical A Aquatic Toxicity Profile is:				mg/L
Acute Effects:	Fish	96-hr LC50		22.0
	Daphnid	48-hr LC50		24.0
	Green algal	96-hr EC50		15.0
Chronic Effects:	Fish	ChV		3.0
	Daphnid	ChV		1.5
	Green algal	ChV		2.0

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Determine Concern Concentration

The next step is translating the predicted endpoints into a freshwater (FW) concern concentration (CC). The following equation is used to calculate the FW CC. The lowest chronic value, the predicted endpoint for Daphnid (1.5 mg/L or ppm), was used. An uncertainty factor (assessment or safety factor) is 10 was used to account for the uncertainty of laboratory to field variation, and as a margin of safety.

$$\begin{aligned} & (\text{Predicted Endpoint} \times 1,000 \text{ conversion from ppm to ppb}) / \text{safety factor} \\ & (1.5 \text{ ppm} \times 1,000) / 10 = 150 \text{ ppb, rounded up to 200 ppb.}^* \end{aligned}$$

*Note: The CC is rounded up to one significant digit to be conservative, and because the safety factor is one significant digit.

Step 2. Estimation Of Surface Water Concentrations

Now that a freshwater CC for Chemical A (200 ppb) has been established, the site-specific release can be evaluated. Assume the following:

- Company ABCDE will discharge 200 kg/day of Chemical A for 300 days per year; and
- There will be 50 percent removal of Chemical A in wastewater treatment.
- The fish BCF value predicted by EPI Suite™ is 175 (not the log BCF)

After talking to Company representatives, the assessor has determined that:

- Company ABCDE discharges to the Little Genesee Creek;
- The NPDES Number is NY0022381.

Using this information the assessor can use the E-FAST model to calculate: the concentration of Chemical A in the Little Genesee Creek; the potential drinking water exposures; and the potential fish ingestion exposure and the potential risk to the aquatic environment.

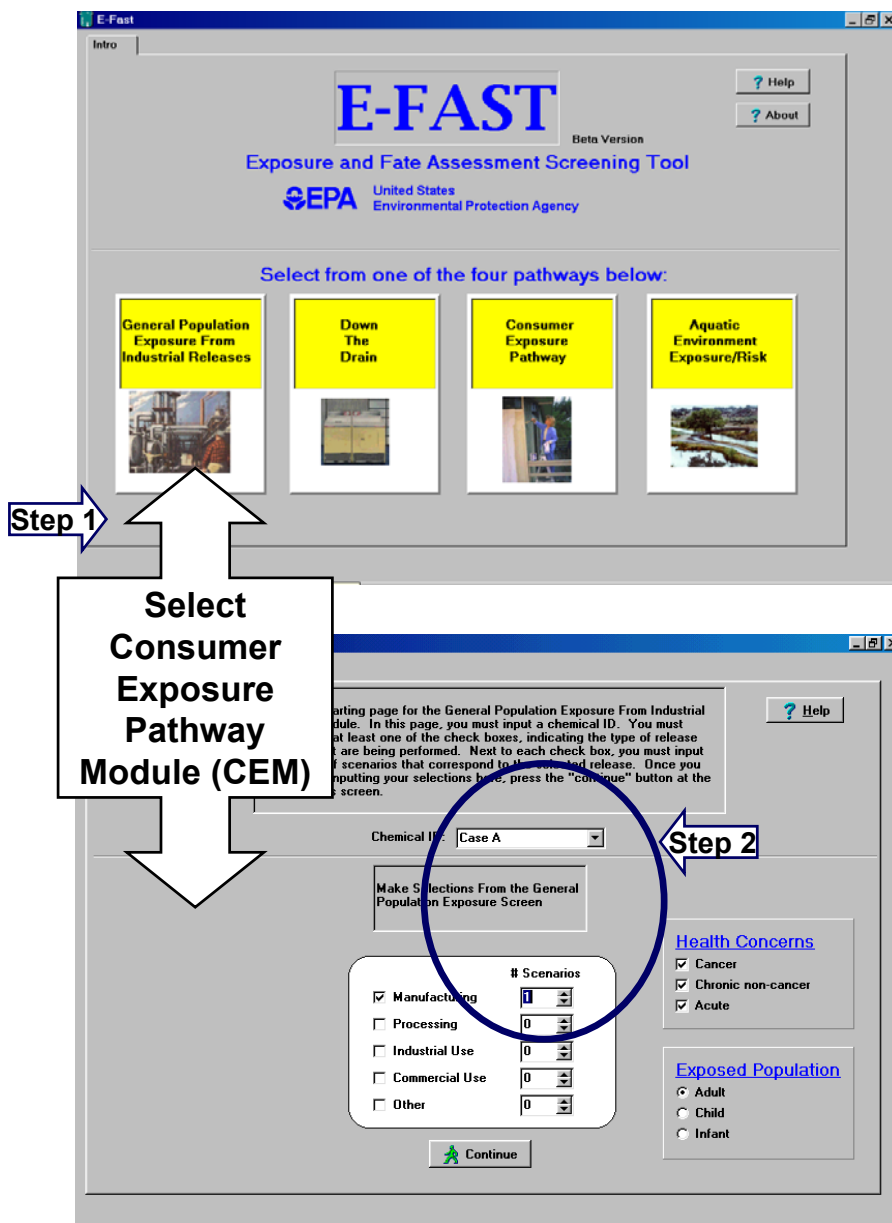
CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module

The following is a step-by-step description of how to run the CEM module.

Once you have entered the E-FAST model:

1. Select: General Population Exposure Module;
2. Enter the chemical identification "Case A", and select 1 Manufacturing Scenario, then click on Continue button.



CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

3. You automatically go to the Release Info page. Put a check in the Surface Water box and add Release Amount (200 kg/site/day) and Release Days per Year (300 days/yr)
4. Click on Facility button. You go to the Select a Facility screen.

E-Fast

Intro | General Pop Exp | **Release Info** | PChem | Exp Factors | Fate

General Release Info | Select a facility | ? Help

Chemicals ID/Rel #
Case A.1

Release Activity
Manufacture

Sites 1

Continue

Select the desired releases and input the amount of release and number of days/year of release if needed

	Release	# Days per year of Release
<input checked="" type="checkbox"/> Surface water	200 kg/site/day	300 days/yr
Choose facility or SIC code analysis:		
<input checked="" type="radio"/> Facility	NPDES #: NY0022381	
<input type="radio"/> SIC Code	Description:	
<input type="checkbox"/> Landfills (including sludge)		
Landfill	0.00 kg/yr	
Sludge	0.00 kg/yr	
<input type="checkbox"/> Ambient air from incineration	0.00 kg/yr	
<input type="checkbox"/> Ambient air from fugitive releases	0.00 kg/site/day	0 days/yr

Step 3

Step 4

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

5. In the Select a Facility screen, type the *NPDES* number (NY0022381) in the proper box. Click on Perform Search for Facility Button. When the search finds the facility, Double click the facility name. Click on Continue button.

The screenshot shows the E-FAST software interface with the 'General Pop Exp' tab selected. The 'Release Information - Facility Selection Screen' is displayed. The 'NPDES' field contains 'NY0022381'. The 'Perform search for facilities' button is visible. Below the search area, a table lists the search results. The first row is highlighted, showing the facility 'BOLIVAR (V) WWTF' with location 'BOLIVAR NY 14715' and reach '05010001025'. A blue arrow labeled 'Step 5' points to the 'BOLIVAR (V) WWTF' facility name in the table.

NPDES	FACILITY NAME	LOCATION	REACH	REACH NAME
NY0022381	BOLIVAR (V) WWTF	BOLIVAR NY 14715	05010001025	LITTLE GENES

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

6. You are sent to the Physical Chemical Properties screen, and you should enter the *BCF* (175) and *Concern Concentration* (200 ppb or $\mu\text{g/L}$). Click on Continue button.

E-Fast

Intro General Pop Exp Release Info PChem Exp Factors Fate

Physical Chemical Properties

Chemical ID: Case A

Bioconcentration Factor 175

Concentration of concern 200 ug/L

☒ High end PDM analysis

☐ Average PDM analysis

Continue

Help

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

7. You are sent to the Exposure Factors Screen where you can review the defaults values. Any of these can be adjusted as necessary. Click on Continue button.

Chemical ID: Case A		
Body weight:	71.80	kg
Exposure duration (cancer):	30.00	years
Exposure duration (non cancer):	30.00	years
Averaging time (cancer):	75.00	years
Averaging time (non cancer):	30.00	years
Drinking water ingestion (chronic):	1.40	L/day
Drinking water ingestion (acute):	6.00	L/day
Fish ingestion (chronic):	6.00	g/day
Fish ingestion (acute):	129.00	g/day
Inhalation rate:	0.55	m3/hr

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

8. You are sent to the Fate Properties Screen where you will enter the percent removal in wastewater treatment (enter 50% for both high and low). Click on Calculate, Save Results, and Display Results button.

E-Fast

Intro General Pop Exp Release Info PChem Exp Factors Fate

Fate Properties

? Help

Chemical ID: Case A

Waste water treatment removal (low): 50 %

Waste water treatment removal (high): 50 %

Drinking water treatment removal: 0.00 %

% removal via incineration: 0.00 %

% removal via fugitive: 0.00 %

Groundwater migration potential: Negligible

Calculate, save results, and display results pages

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

- Environmental Release Results are calculated and you get a message saying the file is saved to the A:\ drive. Click on OK. Click on River tab.

E-FAST

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *PDM Site

Chemicals ID/Rel #
Case A 1

Environmental Release Results

Number of Sites:

	Water	Landfill/Sludge	Incineration	Fugitive
Total Releases: (before treatment)	6.00E+04 (kg/yr)	0.00 (kg/yr)	0.00 (kg/yr)	0.00 (kg/yr)
Release days/yr: (before treatment)	<input type="text" value="300.00"/>			<input type="text" value="0.00"/>
Per site release	<input type="text" value="200.00"/> (kg/site/day)	0.00 (kg/yr)	0.00 (kg/yr)	0.00 (kg/site/day)

Calculations Complete

Final report stored as a:\Case A.exp

OK

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

- Site-Specific Human and Aquatic Exposures to Surface Water Releases - Drinking Water Exposure Estimates Results are displayed. You can click on Fish Ingestion Information to view those exposure estimates.

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *PDM Site

Site-Specific Human And Aquatic Exposures to Surface Water Releases ? Help

Chemicals ID/Rel #: **Case A.1**

Release Activity: **Manufacture** Exposed Population: **Adult**

Facility name: **BOLIVAR (V) WWTF** Discharge Type: **Direct**

Facility location: **BOLIVARNY14715** WWT Removal: **50.00 %**

NPDES#: **NY0022381** Release days: **300.00**

Reach Number: **05010001025** Pre-treatment release: **200.00 kg/day**

Reach Name: **LITTLE GENESEE CR** Post-treatment release: **100.00 kg/day**

Facility on reach? ☒ Yes ☐ No ☐ Unk. Bio Concentration Factor: **175.00 L/kg**

General Site Information | Drinking Water Information | Fish Ingestion Information

Drinking Water Exposure Estimates

Exposure Type	Results	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer					
LADDpot (mg/kg/day)	6.74E-03	30.00	75.00	71.80	1.40
LADCpot (mg/kg)	0.35	30.00	75.00	NA	NA
Chronic Non-Cancer					
ADDpot (mg/kg/day)	1.69E-02	30.00	30.00	71.80	1.40
ADCpot (mg/kg)	0.86	30.00	30.00	NA	NA
Acute					
ADRpot (mg/kg/day)	0.17	1 day	1 day	71.80	6.00

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *PDM Site

Site-Specific Human And Aquatic Exposures to Surface Water Releases ? Help

Chemicals ID/Rel #: **Case A.1**

Release Activity: **Manufacture** Exposed Population: **Adult**

Facility name: **BOLIVAR (V) WWTF** Discharge Type: **Direct**

Facility location: **BOLIVARNY14715** WWT Removal: **50.00 %**

NPDES#: **NY0022381** Release days: **300.00**

Reach Number: **05010001025** Pre-treatment release: **200.00 kg/day**

Reach Name: **LITTLE GENESEE CR** Post-treatment release: **100.00 kg/day**

Facility on reach? ☒ Yes ☐ No ☐ Unk. Bio Concentration Factor: **175.00 L/kg**

General Site Information | Drinking Water Information | Fish Ingestion Information

Fish Ingestion Exposure Estimates

Exposure Type	Results	ED (yrs)	AT (yrs)	BW (kg)	IR (g/day)
Cancer					
LADDpot (mg/kg/day)	5.06E-03	30.00	75.00	71.80	6.00
LADCpot (mg/kg)	60.50	30.00	75.00	NA	NA
Chronic Non-Cancer					
ADDpot (mg/kg/day)	1.26E-02	30.00	30.00	71.80	6.00
ADCpot (mg/kg)	151.25	30.00	30.00	NA	NA
Acute					
ADRpot (mg/kg/day)	0.33	1 day	1 day	71.80	129.00

CASE STUDY A: Potential Aquatic and Human Exposures to Surface Water Discharges from a Manufacturing Facility

Run the E-FAST General Population Exposure Module (continued)

- Click on General Site Information to view Aquatic Exposure Estimates. Click on PDM Site tab to view PDM Site-Specific Aquatic Exposure estimates. Congratulations! You have your results. The CC will be exceeded **240 days per year**.

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *PDM Site

Site-Specific Human And Aquatic Exposures to Surface Water Releases

Chemicals ID/Rel #: **Case A.1**

Release Activity: **Manufacture** Exposed Population: **Adult**

Facility name: **BOLIVAR (V) WWTF** Discharge Type: **Direct**

Facility location: **BOLIVARNY14715** WWT Removal: **50.00 %**

NPDES #: **NY0022381** Release days: **300.00**

Reach Number: **05010001025** Pre-treatment release: **200.00 kg/day**

Reach Name: **LITTLE GENESEE CR** Post-treatment release: **100.00 kg/day**

Facility on reach? ☒ Yes ☐ No ☐ Unk. Bio Concentration Factor: **175.00 L/kg**

General Site Information | Drinking Water Information | Fish Ingestion Information

Aquatic Exposure Estimates - Surface Water

Flow descriptor	Harmonic Mean	30q5	7q10	1q10
Flow (MLD)	95.10	49.94	30.54	25.29
Concentration (ug/L)	1051.57	2002.52	3274.93	3954.12

E-Fast

Intro | General Pop Exp | Release Info | PChem | Exp Factors | Fate | *Env. Rel. | *River | *PDM Site

Chemical ID: **PDM Site Specific Page**

Chemicals ID/Rel #: **Case A.1**

NPDES #: **NY0022381**

Release Activity: **Manufacture** Discharge Type:

Facility name: **BOLIVAR (V) WWTF** WWT Removal: **50.00 %**

Facility location: **BOLIVARNY14715** Release days: **300.00 days/yr**

Reach Number: **05010001025** Concentration of concern: **200.00 ug/L**

Reach Name: **LITTLE GENESEE CR** Pre-treatment release: **200.00 kg/day**

Facility on reach? ☒ Yes ☐ No ☐ Unk. Post-treatment release: **100.00 kg/day**

Mean streamflow: **202.81 MLD**

Low streamflow: **30.54 MLD**

Effluent flow: **1.44 MLD**

PDM Site Specific Estimates

Days exceeded: **239.52**

% year exceeded: **65.62**

Case Study B

Consumer Dermal Exposure

Uses the E-FAST
Consumer Exposure Pathway (CEM) Module

Case Study B: Consumer Exposure from Dermal Contact

Introduction

The purpose of this case study is to assess consumer exposure that may result from dermal contact with a proposed new additive to a consumer product. The Brown Manufacturing Corporation (BMC) is considering using Chemical C as a colorant in a new bar soap product. The BMC risk assessor must estimate potential consumer exposure to Chemical C before BMC product developers can make the decision to proceed with the new formulation. The assessor will use the E-FAST Consumer Exposure Module (CEM) to predict a Potential Lifetime Average Daily Dose (LADD) Rate, a Potential Average Daily Dose (ADD) Rate, and an Acute Potential Dose Rate (APDR) for a consumer from dermal contact with Chemical C in the soap product through hand and body washes.

The BMC risk assessor knows the following information about the proposed product and candidate Chemical C:

- Weight fraction of Chemical C in the final soap product will be 0.0025 - 0.0075 (percent by weight) (median = 0.005); and
- The chronic oral RfD for an adult (70 kg average body weight) for Chemical C is 0.02 mg/kg-day.

Estimation Of APDR, ADD and LADD Using CEM

Enter E-FAST (Figure C1). Proceed with the following steps:

1. Select Consumer Exposure Pathway Module (Figure C2);
2. Select Begin New CEM Run (Figure C2);
3. In the CEM Introduction Screen, enter Chemical Identification Information (Figure C3);
4. Click on the Scenario Tab (Figure C3);
5. Choose Bar Soap (Figure C4);
6. Click on Dermal Inputs Tab and view preset defaults (Figure C5). Any of these defaults can be overridden if necessary.
7. Click on Chemical Properties Tab and enter weight fraction information (Figure C6).
 - Median = 0.005
 - High end (90th%) = 0.0075;
8. Select Run the model (Figure C6).
9. Results are displayed. Click on Outputs-Dermal (Figure C6). Results can be saved in a WP file or printed.

Case Study B: Consumer Exposure from Dermal Contact

CEM Model Results

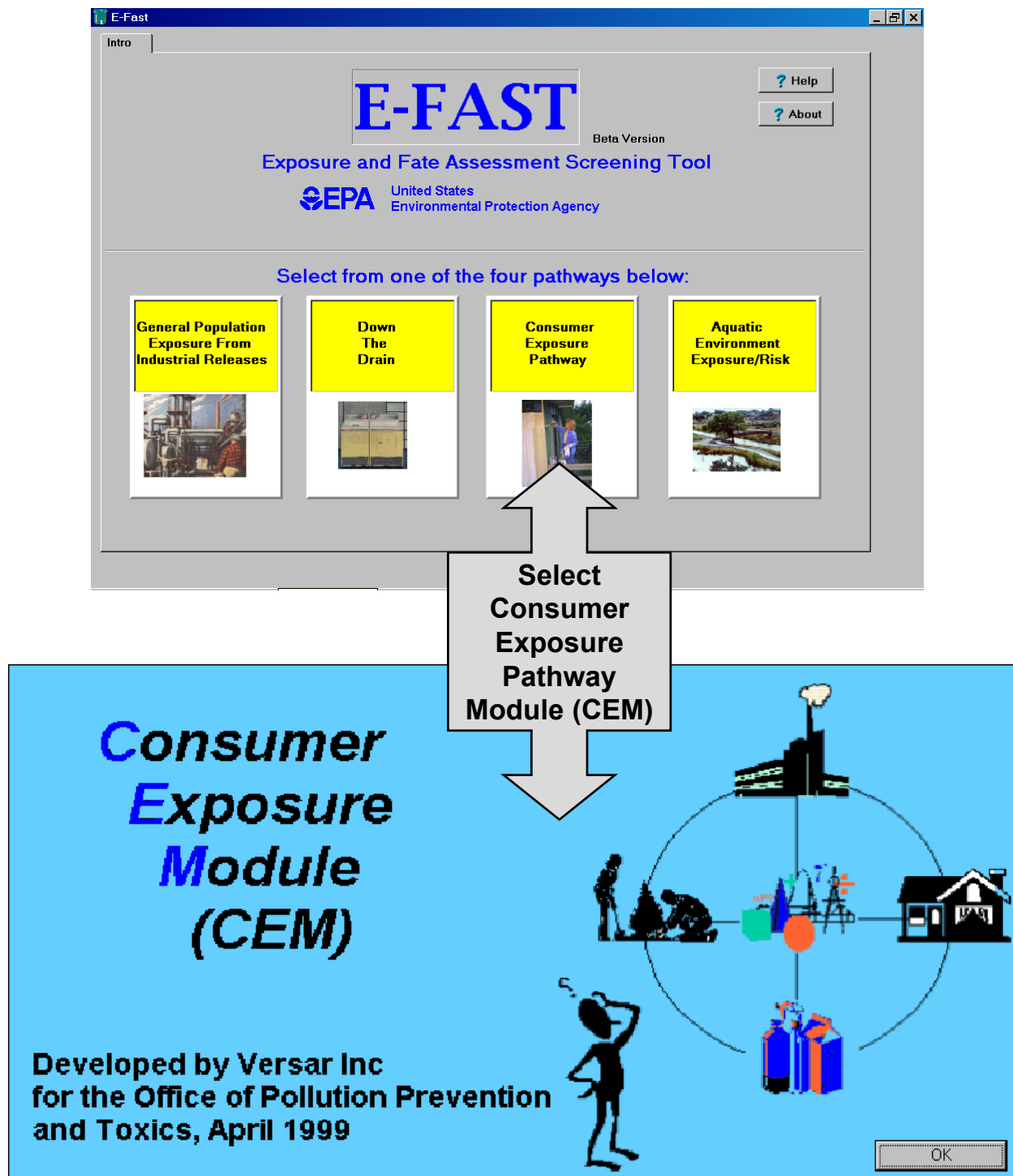
After running the CEM model, the BMC risk assessor obtained the following predicted exposure results (see Figure C6):

LADD	=	2.71e-03 mg/kg-day
ADD	=	2.75e-03 mg/kg-day
APDR	=	4.52e-03 mg/kg-day

In-house studies have demonstrated that the **dermal absorption fraction** of Chemical C is 10 to 20 percent of the applied dose. Using the more conservative value of 20 percent absorption, the assessor will adjust the predicted ADPR 4.52e-03 mg/kg-day to obtain a predicted absorbed adult dose of 8.984e-04 mg/kg-day. This is below the reported adult chronic oral RfD for Chemical C of 2.00e-02 mg/kg-day. The assessor will report to product developers that the amount of Chemical C in the soap formulation will not exceed the chronic oral RfD for Chemical C.

Case Study B: Consumer Exposure from Dermal Contact

Figure C1
E-FAST Opening Screen



Case Study B: Consumer Exposure from Dermal Contact

Figure C2
CEM Opening Screen

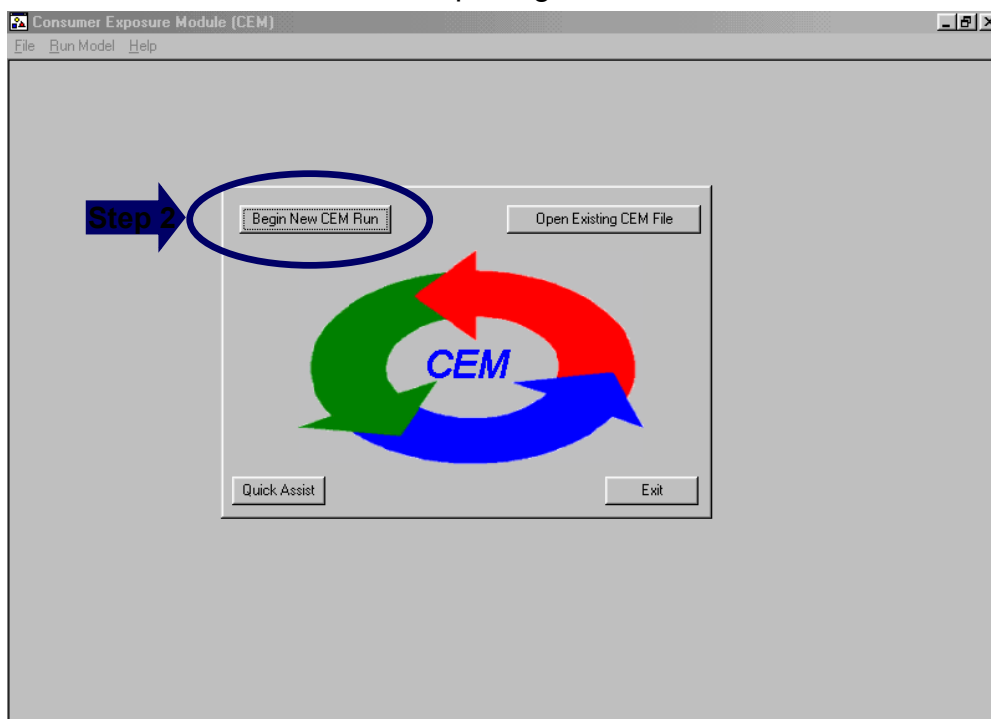
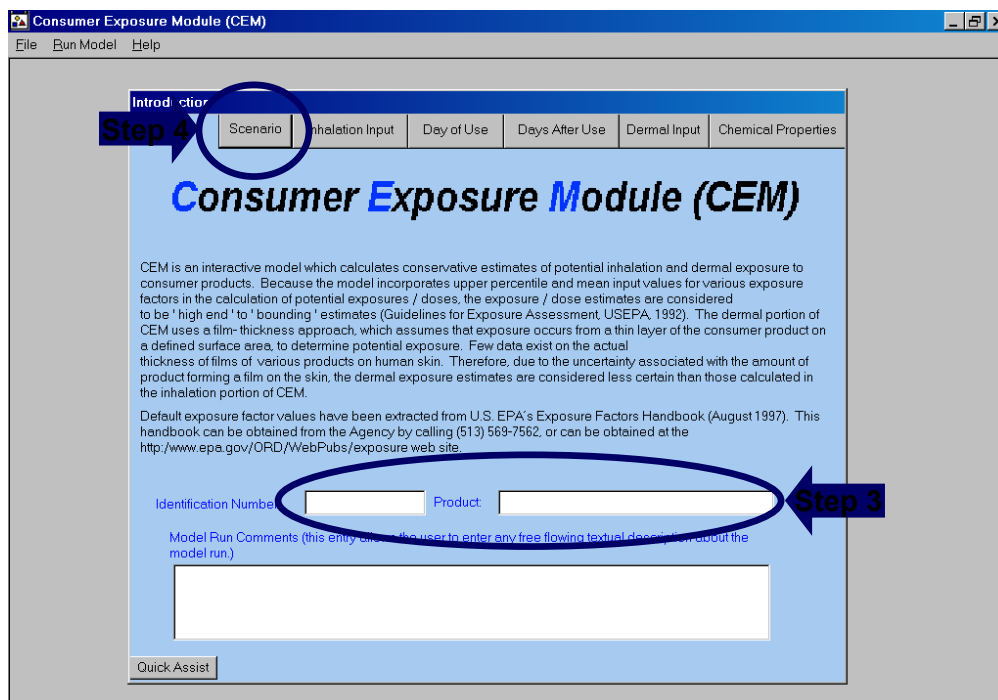


Figure C3
CEM Introduction Screen



Case Study B: Consumer Exposure from Dermal Contact

Figure C4
Dermal Scenario Selection Screen

Consumer Exposure Module (CEM)

File Run Model Help

Scenario Data

Introduction Scenario Inhalation Input Day of Use Days After Use Dermal Input Chemical Properties

Product Applied to Surface (Dermal, Inhalation)

☐ General Purpose Cleaner

☐ Latex Paint

Product Sprayed on Surface (Inhalation)

☐ Fabric Protector

☐ Aerosol Paint

Product Added to Water (Dermal, Inhalation)

☐ Laundry Detergent

Product Placed in Environment (Inhalation)

☐ Solid Air Freshener

Step 5 → ☒ **Product Directly Contacting Skin (Dermal)**

☒ Bar Soap

☐ Used Motor Oil

☐ User Defined Scenario

Age Group: Adult

Quick Assist

Figure C5
Dermal Scenario Input Screen

Consumer Exposure Module (CEM)

File Run Model Help

Dermal Inputs

Introduction Scenario Inhalation Input Day of Use Days After Use **Dermal Input**

Scenario: General Purpose Cleaner

This screen allows the user to input the required product parameters for the dermal model.

Identification Number: Unknown Product: Unknown

Amount Retained on Skin: g/cm2-event Years of Use: years

Frequency of Use: events/year Surface Area to Body Weight Ratio: cm2/kg

Averaging Time - LADD, LADC: years Averaging Time - ADD, ADC: years

Quick Assist

Step 6 →

Case Study B: Consumer Exposure from Dermal Contact

Figure C6
CEM Model Inputs

Consumer Exposure Model (CEM)

File Run Model Help

Chemical Properties

Introduction Scenario Inhalation Input Day of Use Days After Use Dermal Input Chemical Properties

Scenario: Bar Soap

This screen allows the user to input the required physical and chemical properties of the product required for the models.

Identification Number: Unknown Product: Unknown

Chemical Name: Chemical

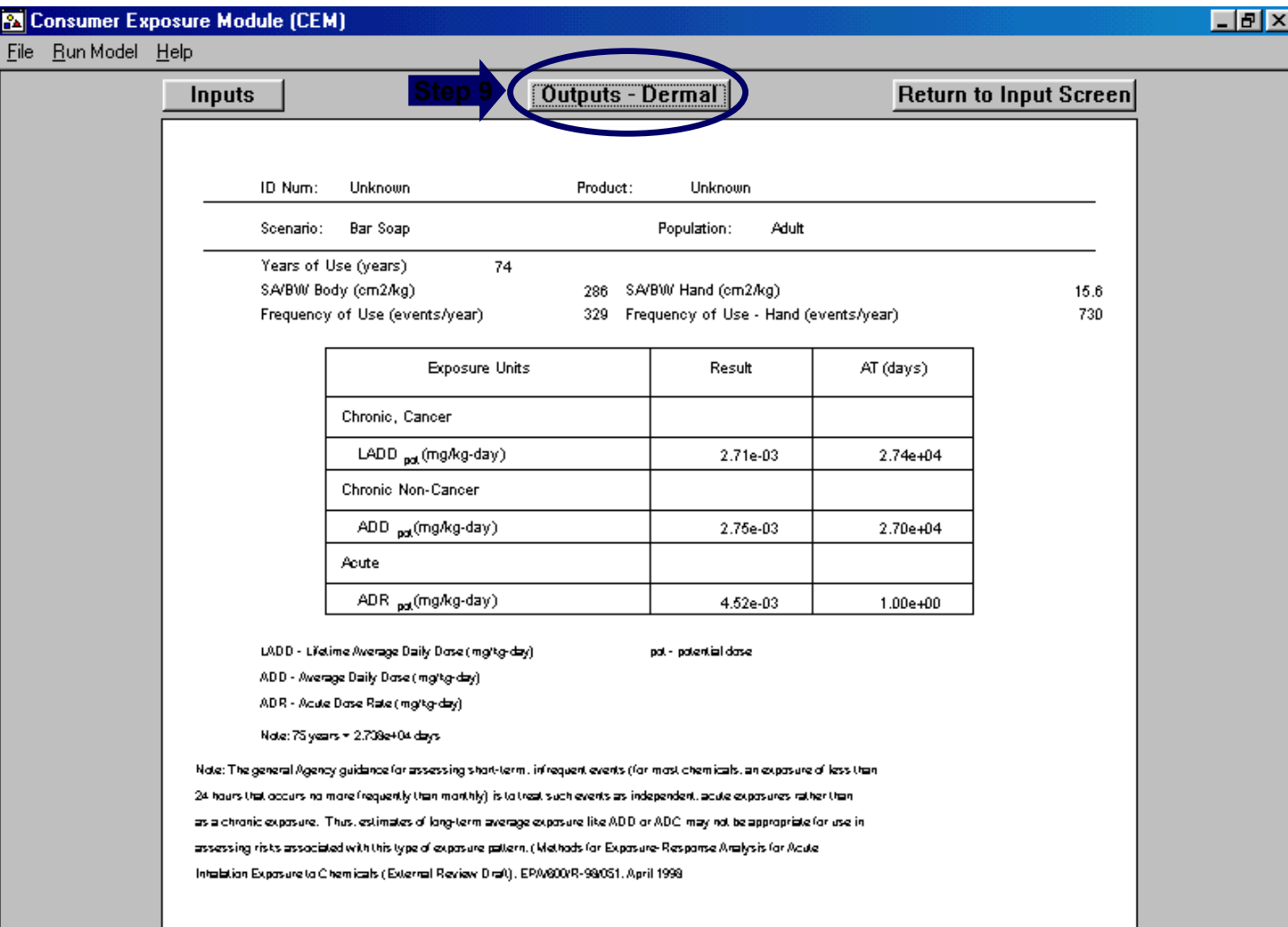
Weight Fraction - Median: 0.005 unitless

Weight Fraction - 90th %: 0.0075 unitless

Quick Assist

Case Study B: Consumer Exposure from Dermal Contact

Figure C6
CEM Model Results



APPENDIX B: Data Sources**APPENDIX B****Data Sources**

NOTE: Before using these P2 Framework Models, or any screening level model, a thorough search for measured data should be conducted. Measured data should be used if available instead of estimated (predicted) data because estimation methods, such as these screening models, contain inherent uncertainties.

The data sources included here are not intended to represent the only or best sources of data available. Readers are strongly encouraged to conduct their own searches for data.

The URLs of certain Internet sites are provided here to provide information to users of the manual. Users are cautioned that due to the dynamic nature of the Internet, these URLs may have been changed from the time of the writing of this document. In case a URL is no longer correct, the user is advised to use any of the search engines to locate the correct URL.

Types of Data Sources included here are:

1. Physical / Chemical Property Data
2. Chemical Human Hazard Data
3. Chemical Environmental Hazard Data
4. Environmental Release Data
5. Exposure Parameter and Population Data

APPENDIX B: Data Sources

Physical / Chemical Property and Fate Data Sources

Beilstein Online <http://www.beilstein.com/products/online/online.shtml> provides access to data on organic compounds. With about 8 million heterocyclic, acyclic and isocyclic compounds, the Beilstein database covers the literature from 1771 onwards. Also available through www.cas.org/ONLINE/DBSS/beilsteinss.html.

BIODEG <http://esc.syrres.com/EFDBInfo.htm> contains experimental values as in CHEMFATE, but only relating to biodegradation subjects. In addition, BIODEG contains evaluation codes that can be used for structure/biodegradability correlations. This file contains over 5,800 records of actual experimental results on biodegradation studies for approximately 800 chemicals. Experimental details, such as chemical concentration and rate of degradation, are included.

BIOLOG <http://esc.syrres.com/EFDBInfo.htm> or the Microbial Degradation/Toxicity File, provides sources of microbial toxicity and biodegradation data. It is more detailed than DATALOG, but does not include experimental values. BIOLOG contains 70,000 records on 8,150 chemicals.

CHEMFATE <http://esc.syrres.com/EFDBInfo.htm> is a data value file with 25 categories of environmental fate and physical/chemical property data on commercially important chemical compounds. Actual experimental values (rate constants, experimental conditions, physical properties, etc.) are abstracted and retained in the file. CHEMFATE contains 17,260 records on 1,728 chemicals. Recommended physical property values were collected for the SARA Section 313 TRI chemicals.

ChemFinder <http://chemfinder.cambridgesoft.com/> online searching by CAS RN or chemical name includes reference databases including The Merck Index, Chemical, Reaction, and Safety databases.

CRC Handbook of Chemistry and Physics www.crcpress.com CRC Handbook of Chemistry and Physics on CD ROM, Version 2003 ISBN: 0849315565

CRC Handbook of Chemistry and Physics: A Ready-Reference Book of Chemical and Physical Data, 78th Edition, 1997. David R. Lide (Editor). CRC Press; ISBN: 0849304784. Handbook contains CAS Registry numbers, and chemical and physical properties.

DATALOG <http://esc.syrres.com/EFDBInfo.htm> is a bibliographic file indexed by Chemical Abstract Service (CAS) registry number that contains eighteen types of environmental fate data. Since individual articles require only cursory examination, no experimental values are entered into the file, and thus, large numbers of chemicals can be rapidly incorporated. This file is the largest in the EFDB, containing 380,000 records on over 16,800 chemicals. DATALOG indicates where environmental fate and exposure data can be found by searching for 18 different properties.

EFHB (Environmental Fate Data Base) <http://esc.syrres.com/EFDBInfo.htm> The EFDB is comprised of several interrelated files, DATALOG, CHEMFATE, BIOLOG, and BIODEG. These databases share a CAS RN file containing over 20,000 chemicals with preferred name and formula, and a bibliographic file containing full references on over 36,000 articles cited.

Envirofate contains data on approximately 800 chemicals. Envirofate contains summary information concerning the environmental fate and the physical-chemical properties of chemicals released into the environment. Chemicals selected for inclusion in the database are produced annually in excess of one million pounds. ENVIROFATE contains twenty-four types of data extracted from papers published worldwide dealing with environmental fate and behavior studies. It is available through CIS (Chemical Information System) www.nisc.com/cis/ (fee).

APPENDIX B: Data Sources

Physical / Chemical Property and Fate Data Sources (continued)

Gmelin Handbook of Inorganic and Organometallic Chemistry

<http://www.beilstein.com/products/xfire/gmelin.shtml> covers organometallic & inorganic compounds.

The Gmelin database covers more than 1.4 million organometallic and inorganic compounds (including coordination compounds, alloys, glasses, ceramics, polymers and minerals), with more than 800 property fields defined.

Handbook of Environmental Fate and Exposure Data for Organic Chemicals. 1997. P.H. Howard (ed.) Vol V. Solvents III. SRC Handbooks Series. CRC/Lewis Publishers, Boca Raton, FL.

Handbook of Environmental Fate and Exposure Data for Organic Chemicals. 1992. P.H. Howard (ed.) Vol IV. Solvents II. SRC Handbooks Series. Lewis Publishers, Chelsea, MI.

Handbook of Physical Properties of Organic Chemicals. PHYSPROP. Howard, P.H.; Meylan, W.M. 1997. CRC/Lewis Publishers, Boca Raton, FL. There is also a database version.

Handbook of Property Estimation Methods for Chemicals. 2000. Boethling, R.S. and MacKay, D. Environmental Health Sciences. Lewis Publishers. Washington, D.C.

Handbook of Environmental Fate and Exposure Data for Organic Chemicals. 1990. P.H. Howard (ed.) Vol II. Solvents. SRC Handbooks Series. Lewis Publishers, Chelsea, MI.

Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds, 1990. Warren J. Lyman, William F. Reehl, and David H. Rosenblatt. American Chemical Society; ISBN: 0841217610. Contains methods for estimating density, vapor pressure, water solubility, and other chemical properties relevant to environmental fate.

Handbook of Environmental Data on Organic Chemicals, 3rd Edition, 1997. Karel Verschueren (Editor). John Wiley & Sons; ISBN: 0471286591. An extensive text compiling information on organic products. The data given include physical properties; e.g., formula, physical appearance, molecular weight, melting point, boiling point, vapor pressure, and solubility.

Handbook of Environmental Degradation Rates. Howard, P.H.; Boethling, R.S.; Jarvis, W.F.; and Meylan, W. 1991. New York: Lewis Publishers, Inc. ISBN: 0873713583.

Handbook of Environmental Fate and Exposure Data for Organic Chemicals. 1989. P.H. Howard (ed.) Vol I. Large Production and Priority Pollutants. SRC Handbooks Series. Lewis Publishers, Chelsea, MI.

Handbook of Environmental Fate and Exposure Data for Organic Chemicals. 1991. P.H. Howard (ed.) Vol III. Pesticides. SRC Handbooks Series. Lewis Publishers, Chelsea, MI.

Hawley's Condensed Chemical Dictionary, 13th Edition, 1997. Gessner Goodrich Hawley (Editor), and Richard J., Sr. Lewis (Editor). John Wiley & Sons; ISBN: 0471292052. (A CD-ROM version is also available). A compendium of technical data and descriptive information covering many thousand chemicals, including their industrial uses, and trademark names.

Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals: Volume V– Pesticide Chemicals, by Donald Mackay, Wan-Ying Shiu, Kuo-Ching Ma. Boca Raton, FL, Lewis Publishers, 1997. 812p., bibliog., index. ISBN 1-56670-255-0.

APPENDIX B: Data Sources**Physical / Chemical Property and Fate Data Sources (continued)**

Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals. Vol I and II. 1992. MacKay, D.; Shiu, W.Y; and Kuo, C.M. Lewis Publishers. New York.

Kirk-Othmer Concise Encyclopedia of Chemical Technology, 3rd Edition, 1989. Martin Grayson (Contributor), Herman F. Mark, and Donald F. Othmer. John Wiley & Sons; ISBN: 0471517003. Provides a concise yet comprehensive summary of various topics in applied aspects of chemistry & chemical engineering. It emphasizes the application of chemistry and chemical engineering to industrially important concepts, products, processes and uses. It provides references for further reading on each of these topics. <http://www.mrw.interscience.wiley.com/kirk/>

Lange's Handbook of Chemistry. 15th Edition. McGraw-Hill, 1999. Known Lange's Handbook, this classic reference covers the entire field of chemistry.

Merck Index: An Encyclopedia of Chemicals, Drugs, & Biologicals by M.J. O'Neil (Editor), et al Publisher: Merck & Co; ISBN: 0911910131; 13th edition (October 2001). A one-volume encyclopedia of chemicals, drugs and biologicals. Contains basic property data such as molecular weight, physical and toxicity data, chemical structures, and commercial uses.

Merck Index 13th CD-ROM Edition <http://products.camsoft.com/ProdInfo.cfm?pid=231> This stand-alone edition contains all the information in The Merck Index 13th Edition.

APPENDIX B: Data Sources

Chemical Human Hazard Data Sources

Agency for Toxic Substances and Disease Registry (ATSDR) www.atsdr.cdc.gov/toxpro2.html contains toxicological profiles of hazardous chemicals most often found at facilities on CERCLA's National Priority List.

CAS (Chemical Abstracts Service) <http://www.cas.org> a division of the American Chemical Society, provides fee-based online access to databases of chemical information. A useful method of searching is through CAS's Science and Technology Network (STN) that searches numerous databases of chemical information.

CCRIS http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?CCRIS Chemical Carcinogenesis Research Information System contains carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition data provided by the National Cancer Institute (NCI).

CHEMEST <http://www.agnic.nal.usda.gov/agdb/chemest.html> contains data for estimating the properties and chemicals of environmental concern. Available through Technical Database Services, Inc.

CHEMFATE <http://esc.syrres.com/efdb/Chemfate.htm> contains evaluated physical property values, rate constants and monitoring concentrations for approximately 1,730 commercially significant compounds.

ChemFinder <http://chemfinder.cambridgesoft.com/> contains synonyms, structure, and physical chemical properties and a link to measured data from Merck Index.

Chemical Categories Document <http://www.epa.gov/opptintr/newchemicals/chemcat.htm> Developed under the New Chemicals Program within EPA's Office of Prevention, Pesticides, and Toxic Substances (OPPT), includes summaries of chemical categories developed to facilitate the review process of new chemicals (Premanufacture Notices) under TSCA Section 5. It is not intended to be a comprehensive list of all chemical substances. EPA's PBT Profiler screening model www.pbtprofiler.net also searches the structure of the chemical entered and identifies any structures present in the chemical that are described in the Chemical Categories Document.

CHEMID - Contains chemical names, synonyms, molecular formulas and CAS numbers. Available through Internet Grateful Med at <http://igm.nlm.nih.gov/>

ChemIDplus <http://chem.sis.nlm.nih.gov/chemidplus/setupenv.html> This software allows for viewing and searching the NLM databases by numerous chemical synonyms, structures, regulatory list information, and contains links to other databases containing information about the chemicals. Using ChemIDplus and ISIS/Draw www.mdl.com/products/isisdraw.html databases searches can be conducted by name, CAS Registry Number, or by structure and substructure. Of the 350,000 records, about one-third have identified structures in the record. Using the (sub)structure searching, non-cancer health effects for structural analogues to the chemical(s) of concern can be identified.

DART/ETIC (Developmental and Reproductive Toxicology and Environmental Teratology) Information Center http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?DARTETIC Contains current and older literature on developmental and reproductive toxicology.

EMIC (Environmental Mutagen Information Center) http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?EMIC contains mutagenicity data.

APPENDIX B: Data Sources

Chemical Human Hazard Data Sources (continued)

GENE-TOX http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?GENETOX GENE-TOX contains peer-reviewed mutagenicity test data from the U.S. EPA.

Health Effects Assessment Summary Tables (HEAST). 1997. U.S. EPA. Contains RfD, RfC, unit risk, and slope factor values for selected chemicals. Available through the National Technical Information Service (NTIS) www.ntis.gov Doc. Number OERR 9200.6-303 (97-1).

Health Assessment Documents (HAD) U.S. EPA. Reviews health effects of specific chemicals.

HSDB - Hazardous Substance Databank http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?HSDB This is an on-line database containing scientifically peer-reviewed data on a chemical properties and fate, human, animal and environmental toxicity, environmental fate, regulations, and treatments. This database is available through TOXNET at <http://toxnet.nlm.nih.gov>; through STN International at www.cas.org/stn.html; and through CCINFOWeb at <http://ccinfoweb.ccohs.ca/>

IRIS http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?IRIS Integrated Risk Information System contains data used by the U.S. EPA in support of human health risk assessment, focusing on hazard identification and dose-response assessment.

IRIS (Integrated Risk Information System). U.S. EPA. Reviews studies used in the derivation of RfD, RfC, unit risk, and slope factor values. A web prototype is available on the Internet at www.epa.gov/ngispgm3/iris

IUCLID http://ecb.jrc.it/existing_chemicals/ International Uniform Chemical Information Database (IUCLID) is the basic tool for data collection and evaluation within the EU-Risk Assessment Programme. IUCLID contains CAS RN, physical / chemical data, toxicology, environmental toxicity and fate information on HPV Chemicals.

MEDLINE is a database of over 11 million article references published in more than 4300 biomedical journals and magazines, and can be searched for free using NLM's PubMed search system. <http://medlineplus.gov>

MEDLINEplus contains pages of carefully selected links to Web resources with authoritative health information, including dictionaries, directories, organizations, news sources and 400 health topics. <http://medlineplus.gov/>

National Library of Medicine Online Data Sources. A very useful online source of health effects data is the National Library of Medicine web site, which has many databases that can be searched through TOXNET <http://toxnet.nlm.nih.gov/>

National Institute of Occupational Safety and Health (NIOSH). Presents Health Hazard Evaluations and Industry-wide Studies. Contains literature reviews of occupational exposure data, health effects data, and animal studies. Rationale are presented for the derivation of NIOSH exposure levels. www.cdc.gov/niosh/homepage.html

National Institute of Occupational Safety and Health (NIOSH) www.cdc.gov/niosh/homepage.html presents health hazard evaluations and industry-wide studies. Contains literature reviews of occupational exposure data, health effects data, and animal studies. Rationale are presented for the derivation of NIOSH exposure levels.

APPENDIX B: Data Sources

Chemical Human Hazard Data Sources (continued)

NLM Gateway (<http://gateway.nlm.nih.gov/gw/Cmd>) another useful source on the NLM's web site, allows users to search NLM databases using multiple retrieval systems. As of June 2002 Gateway searches MEDLINE, PubMed, and MEDLINEplus.

Patty's Industrial Hygiene and Toxicology, Vols. 1-4. John Wiley & Sons. (CD-ROM version is available). Contains toxicology and properties of selected industrial chemicals and classes of chemicals.

PHYSPROP - The Physical Properties Database (PHYSPROP) contains chemical structures, names and physical properties for over 25,070 chemicals. This information is available at the Syracuse Research Corporation (SRC) web site at <http://escplaza.syrres.com/interkow/PhysProp.htm>

PubMed is a Web-based search system, produced by NLM's National Center for Biotechnology Information (NCBI), which allows users to access a superset of NLM's MEDLINE database containing MEDLINE, in-process citations and articles from selectively indexed journals that normally would not be selected for MEDLINE indexing. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

STN International www.cas.org/stn.html and CCINFOWeb <http://ccinfoweb.ccohs.ca/aboutCCINFOWeb.html> contain information on chemical abstracts, CAS numbers, molecular formulas, reaction information, chemical indexing, etc.

TOXLINE http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?TOXLINE Contains an extensive array of references to literature on biochemical, pharmacological, physiological, and toxicological effects of drugs and other chemicals.

TSCATS. Provides public access to information submitted to U.S. EPA under the various sections of TSCA (Toxic Substances Control Act). TSCATS is available from several on-line sources (CIS, NLM) or on the Internet at www.rtk.net/www/data/tsc_all.html or <http://esc.syrres.com/efdb/TSCATS.htm>

APPENDIX B: Data Sources**Chemical Environmental Hazard Data Sources**

Acute Toxicity of Organic Chemicals to Fathead Minnows (*Pimephales promelas*), Vols. 1-5. Brooke, L.T., D.J. Call, D.L. Geiger and C.E. Northcott, Eds. 1984-1990. This is a comprehensive source of measured fish toxicity values for a single species (fathead minnows), including fish LC50 data.

Ambient Water Quality Criteria Documents. U.S. EPA. Contains aquatic toxicity values chemicals for which ambient water quality criteria have been developed, and is useful for organic and inorganic compounds. www.epa.gov/waterscience/pc/ambient.html

AQUIRE (Aquatic Information Retrieval) - Contains data extracted from published literature worldwide and from independently compiled data files; includes data on acute and chronic toxicity, bioaccumulation, and sublethal effects data from tests performed on freshwater and saltwater species. AQUIRE is accessible through CIS (Chemical Information System), EPA's Office of Research and Development; and the entire AQUIRE database can be downloaded from www.epa.gov/medecotx/data_download/aquire/aquire_ascii_download.htm

ChemID - Maintained by the National Library of Medicine (NLM); serves as an authority file for the identification of chemical substances cited in NLM databases. Contains chemical names, synonyms, molecular formulas and CAS numbers. Available through Internet Grateful Med at <http://igm.nlm.nih.gov/>

CIS (Chemical Information System) www.nisc.com/cis/ (fee) - 30 databases concerned with chemicals having an environmental impact or that are regulated in some way. Originally developed by the National Institutes of Health and EPA for managing chemical data and information, CIS is now owned by Oxford Molecular.

CTA (Catalog of Teratogenic Agents) - Emphasizes human data and covers pharmaceuticals, chemicals, environmental pollutants, food additives, household products, and viruses; substances are listed alphabetically, and each entry briefly summarizes research procedures and results. The Catalog is accessible as a database through CIS (Chemical Information System) www.nisc.com/cis/ (fee)

CCRIS (Chemical Carcinogenesis Research Information System) - Contains data derived from carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition studies; contains over 8,000 chemical records and is sponsored by the National Cancer Institute. The database is available through CIS (Chemical Information System) and the National Library of Medicine's TOXNET system. www.nlm.nih.gov/pubs/factsheets/ccrisfs.htm

DART (Development and Reproductive Toxicology) http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?DARTETIC and ETICBACK (Environmental Teratology Information Center Backfile) - DART is a bibliographic database covering literature on teratology and other aspects of developmental toxicology. It is managed by NLM and funded by EPA, the National Institute of Environmental Health Sciences (NIEHS), and the National Center for Toxicological Research of the Food and Drug Administration. DART is a continuation of ETICBACK, which contains 49,000 citations to teratology literature published from 1950-1989.

DATALOG - Contains citations for published articles containing data on the environmental fate and the physical-chemical properties of chemicals released into the environment. Available through CIS (Chemical Information System) www.nisc.com/cis/ (fee)

APPENDIX B: Data Sources

Chemical Environmental Hazard Data Sources (continued)

EMIC (Environmental Mutagen Information Center) http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?EMIC and EMICBACK (Environmental Mutagen Information Center Backfile) - EMIC is a bibliographic database containing some 20,000 citations to literature on chemical, biological, and physical agents that have been tested for genotoxic activity. It is produced by the Oak Ridge National Laboratory (ORNL) and funded by EPA and NIEHS. EMIC covers literature published since 1991. EMICBACK contains over 75,000 citations to literature published from 1950-1990.

Envirofate - Contains summary information from papers published worldwide on the environmental fate and the physical-chemical properties of chemicals released into the environment; chemicals included are those produced annually in excess of one million pounds; available through CIS (Chemical Information System) www.nisc.com/cis/ (fee)

GENE-TOX (Genetic Toxicology) http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?GENETOX GENE-TOX Contains genetic toxicology test results on over 3,000 chemicals. Selected mutagenicity assay systems and the source literature are reviewed by work panels of scientific experts for each of the test systems under evaluation. The GENE-TOX data bank is the product of these data review activities. Each test system in GENE-TOX has been peer reviewed and is referenced.

Handbook of Environmental Data on Organic Chemicals, 3rd Edition, 1997. Karel Verschueren (Editor). John Wiley & Sons; ISBN: 0471286591. An extensive text compiling information of organic products. The data given include physical properties: e.g., formula, physical appearance, molecular weight, melting point, boiling point, vapor pressure, and solubility.

HSDB (Hazardous Substances Data Bank) http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?HSDB [Discussed in "Physical / Chemical Property And Fate Data Sources"]

IRIS (Integrated Risk Information System) <http://www.epa.gov/iris> Prepared and maintained by EPA, IRIS is an electronic database containing health risk and EPA regulatory information on specific chemicals. IRIS was developed by EPA staff in response to a growing demand for consistent risk information on chemicals substances for use in decision-making and regulatory activities. IRIS is designed for EPA staff, but is also accessible to state and local environmental health agencies. The information in IRIS is intended for EPA staff with extensive training in toxicology, but with some knowledge of health sciences. The database can also be searched online through the TOXNET system. List of IRIS Substances at <http://www.epa.gov/docs/ngispgm3/iris/subst/index.html>

Merck Index - Encyclopedia of chemicals, drugs, pesticides, and biologically active substances; is available in both print and electronic versions. The online database, which is available through CIS (Chemical Information System) and DIALOG, contains nearly 10,000 records containing references to approximately 30,000 substances, inclusive dates late 19th century to present, updated semi-annually, produced by Merck & Co., Inc.

NIOSH (National Institute for Occupational Safety and Health) - established by the Occupational Safety and Health Act of 1970; is part of the Centers for Disease Control and Prevention (CDC); is the only federal Institute responsible for conducting research and making recommendations for the prevention of work-related illnesses and injuries. NIOSHTIC and RTECS are both produced by NIOSH. <http://www.cdc.gov/niosh/homepage.html>

APPENDIX B: Data Sources

Chemical Environmental Hazard Data Sources (continued)

NIOSHTIC - the National Institute for Occupational Safety and Health's (NIOSH) electronic, bibliographic database of literature in the field of occupational safety and health. NIOSHTIC is updated quarterly and is available online and on compact disk from several vendors. Information contained within NIOSHTIC is selected from a number of sources. NIOSHTIC is accessible as a subfile in the TOXLINE database. <http://www.cdc.gov/niosh/nioshtic.html#NTIC4>

NLM (National Library of Medicine) <http://sis.nlm.nih.gov/> One of the national libraries of the United States, located on the campus of the National Institutes of Health, it provides a number of services and resources for use by the American public. Fact sheets on NLM's toxicological databases are at http://sis.nlm.nih.gov/tox_chart.htm

NTP (National Toxicology Program) conducts toxicity/carcinogenesis studies on agents suspected of posing hazards to human health; data on more than 800 chemical studies are on file. NTP Information is routinely provided to industry and the public on an as requested basis. National Toxicology Program Technical Reports at <http://ehis.niehs.nih.gov/ntp/docs/ntp.html> (fee). The National Toxicology Program Web site is http://ntp_server.niehs.nih.gov/Main_Pages/Chem_HS.html NIEHS Environmental Health Information Service (EHIS) is http://ehis.niehs.nih.gov/ntp/docs/chem_hs.html (fee)

PHYTOTOX - Contains data from the open literature on the effects of the application of one concentration of a single organic chemical on a particular terrestrial vascular plant species. Phytotox is available through CIS (Chemical Information System) www.nisc.com/cis/, as well as through EPA's Office of Research and Development.

RTECS (Registry of Toxic Effects of Chemical Substances) - Contains over 100,000 records covering 1971 to present, quarterly updates, maintained by NIOSH; is a comprehensive database of toxic effects and general toxicology reviews, data on skin and/or eye irritation, mutation, reproductive consequences, and tumorigenicity are provided. Toxic effects are linked to literature citation from both published and unpublished government reports (including unpublished test data from TSCATS, the EPA TSCA test submissions database), and published articles from the scientific literature. RTECS database is available from a number of vendors and can be accessed via the TOXNET at <http://toxnet.nlm.nih.gov>

SANSS GREENCARD (Structure and Nomenclature Search System) - www.nisc.com/cis/details/sanss.htm contains records for more than 500,000 chemicals, is an index to most of the other CIS (Chemical Information System) www.nisc.com/cis/ Components/databases as well as to over 100 other important sources of information on environmentally significant chemicals; is a pointer to CIS sources such as RTECS, the Merck Index, and AQUIRE, as well as non-CIS sources such as IARC Monographs, Hazardous Substances Data Bank, and National Toxicology Program studies.

Subchronic Toxicity of Industrial and Agricultural Chemicals to Fathead Minnows (*Pimephales promelas*), Volume 1. S Call, D.J. and D.L. Geiger, Eds. 1992. source of measured fish toxicity values for a single species (fathead minnows), including fish EC50 data.

Toxicity of Power Plant Chemicals to Aquatic Life. 1973. Presents aquatic toxicity values for organic and inorganic chemicals used by power plant. U.S. Atomic Energy Commission.

APPENDIX B: Data Sources

Chemical Environmental Hazard Data Sources (continued)

TOXLINE http://toxnet.nlm.nih.gov/cgi_bin/sis/htmlgen?TOXLINE the National Library of Medicine's extensive collection of online bibliographic information covering the biochemical, pharmacological, physiological, and toxicological effects of drugs and other chemicals. TOXLINE and its backfile TOXLINE65 together contain more than 2.5 million bibliographic citations, almost all with abstracts and/or indexing terms and CAS Registry Numbers. The information in TOXLINE is taken from secondary sources which formulate the subfiles listed below. Citations with publication year 1980 and older are located in the backfiles.

TOXNET (TOXicology Data NETwork) is a computerized system of files oriented to toxicology and related areas. It is managed by the National Library of Medicine's (NLM) Toxicology and Environmental Health Information Program (TEHIP) and runs on Sun servers in a UNIX-based environment. <http://toxnet.nlm.nih.gov> TOXNET Web interface also allows users to search for toxicology data in the following toxicology data files: Hazardous Substances Data Bank, Chemical Carcinogenesis Research Information System, Integrated Risk Information System, and GENE-TOX, as well as EPA's Toxics Release Inventory (TRI).

TSCATS (Toxic Substances Control Act Test Submissions) - Data submitted by industry to EPA under several provisions of the Toxic Substances Control Act, TSCATS database indexes these submissions, which include unpublished health and safety studies, chemical test data, and substantial risk data submitted to EPA under TSCA sections 4, 8(d), 8(e), and FYI. The actual studies can be purchased from the National Technical Information Service (NTIS) for a fee and CIS (Chemical Information System). TSCATS is available from several on-line sources (CIS, NLM), on the Internet at www.rtk.net/www/data/tsc_all.html or <http://esc.syrres.com/efdb/TSCATS.htm> TSCATS can be viewed on microfiche in the TSCA Non-Confidential Information Center (the TSCA Docket).

APPENDIX B: Data Sources

Environmental Release Data Sources

AQS (The Air Quality System) database <http://www.epa.gov/air/data/aqsdb.html> contains measurements of "criteria air pollutant" concentrations in the 50 United States, plus the District of Columbia, Puerto Rico, and the Virgin Islands.

Chemical Engineering Branch Manual for the Preparation of Engineering Assessments. 1991. U.S. EPA. Conducted by IT Environmental Programs for Office of Toxic Substances (OTS) under Contract No. 68-D8-0112. Washington D.C.

ISDB (Industry Studies Database). U.S. EPA. Contains survey data collected by the Office of Solid Waste (OSW) covering both RCRA and non-RCRA wastes generated by 470 facilities in 11 industries. The data include company identify and location, SIC code, product name, production volume, waste stream properties and category, constituents and their concentrations in the waste stream, management practice and location, and quantity of waste stream.

Kirk-Othmer Concise Encyclopedia of Chemical Technology, 3rd Edition, 1989. Martin Grayson (Contributor), Herman F. Mark, and Donald F. Othmer. John Wiley & Sons; ISBN: 0471517003. This is a comprehensive source of chemical synthesis processes.
<http://www.mrw.interscience.wiley.com/kirk/>

Office of Water Effluent Limitations Guidelines and Standards (for selected industries).
<http://cfpub.epa.gov/npdes/techbasedpermitting/effguide.cfm>

PCS (The Permit Compliance System) is an information management system maintained by the U.S. EPA's Office of Wastewater Enforcement and Compliance (OWEC), to track the permit, compliance, and enforcement status of facilities regulated by the National Pollutant Discharge Elimination System (NPDES). PCS tracks information about wastewater treatment, industrial, and Federal facilities discharging into navigable waters. <http://www.epa.gov/enviro/> or http://www.epa.gov/enviro/html/pcs/pcs_overview.html#PCS

TRI (Toxic Chemical Release Inventory) Files - TRI contains information on the annual estimated releases of toxic chemicals to the environment. It is mandated by the Emergency Planning and Community Right-to-Know Act and is based upon data submitted to the Environmental Protection Agency (EPA) from industrial facilities throughout the U.S.A. This data includes names and addresses of the facilities, and the amounts of certain toxic chemicals they release to the air, water, or land, or transfer to waste sites. Information is included on over 600 chemicals and chemical categories. Separate TRI files are available for each year beginning with 1987. Since 1991, pollution prevention data are also reported by each facility for each chemical. <http://www.epa.gov/enviro/> or <http://www.epa.gov/tri/>

Published chemical monitoring data reports.

Company product literature.

APPENDIX B: Data Sources

Exposure Parameter Data Sources

Exposure Factors Handbook. 1996. Exposure Factors Handbook: V.I General Factors EPA/600/P-95/002Ba; V.II Food Ingestion Factors EPA/600-P-95/002Bb; V.III Activity Factors EPA/600/P-95-002Bc August 1996. U.S. EPA. Presents a summary of available data on human behaviors and characteristics which affect exposure to environmental contaminants and presents recommended values to use for these factors. It provides factor data on ingestion rates of foods, water, breast milk, and soil; factors for inhalation and dermal exposure; data for body weight, lifetime, activity factors; data for use of consumer products; and data for exposures that occur in residences. Available in pdf format at www.epa.gov/ORD/WebPubs/exposure/

Methods for Assessing Exposure to Chemical Substances. U.S. EPA. 1985. Office of Toxic Substances (OTS). Prepared by Versar, Inc. under EPA Contract No. 68-01-6271. Washington DC. These methods described in these volumes were identified by OTS (now officially OPPT) as having utility in exposure assessments on existing and new chemicals under the OTS program. The title of the basic volumes are as follows*:

- V. 1. Methods for Assessing Exposure to Chemical Substances. (EPA 560/5-85-001).
- V. 2. Methods for Assessing Exposure to Chemical Substances in the Ambient Environment. (EPA 560/5-85-002).
- V. 3. Methods for Assessing Exposure from Disposal of Chemical Substances (EPA 560/5-85-003).
- V. 4. Methods for Enumerating and Characterizing Populations Exposed to Chemical Substances (EPA 560/5-85-003).
- V. 5. Methods for Assessing Exposure to Chemical Substances in Drinking Water (EPA 560/5-85-005).
- V. 6. Methods for Assessing Occupational Exposure to Chemical Substances (EPA 560/5-85-006).
- V. 7. Methods for Assessing Consumer Exposure to Chemical Substances (EPA 560/5-85-007).
- V. 8. Methods for Assessing Environmental Pathways of Food Contamination (EPA 560/5-85-008).
- V. 9. Methods for Assessing Exposure to Chemical Substances Resulting from Transportation-Related Spills (EPA 560/5-85-009).
- V. 11. Methods for Estimating the Migration of Chemical Substances from Solid Matrices (EPA 560/5-85-015).
- V. 13. Methods for Estimating Retention of Liquids on Hands (EPA 560/55-85-017).

*Volumes 10 and 12 were not issued.

Population Data Sources

Census of Population Reports. U.S. Bureau of the Census. Available from the U.S. Bureau of the Census on CD-ROM and on the Internet. Populations are characterized geographically by social and economic characteristics, and also by housing characteristics. www.census.gov

Methods for Enumerating and Characterizing Populations Exposed to Chemical Substances. Volume 4. U.S. EPA. Presents methods and data sources for identifying and characterizing populations of interest.

APPENDIX C: Summary of Writing SMILES Notations

SMILES: (Simplified Molecular Input Line Entry System)

What is SMILES?

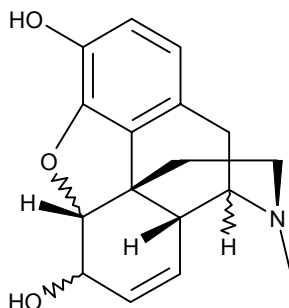
SMILES is "Simplified Molecular Input Line Entry System," which translates a chemical's structure into a string of symbols that is easily understood by computer software. SMILES notation are used to enter chemical structure into EPI Suite™ estimation programs and ECOSAR. Additional examples of SMILES notations are available in the HELP files of EPI Suite™ and ECOSAR. Software programs are available which can translate a chemical structure into SMILES.

References:

Weininger, D. 1988. SMILES, a Chemical and Information System. 1. Introduction to Methodology and Encoding Rules. J. Chem. Inf. Comput. Sci. 28(1): 31-6.
 Wiswesser, W.J. 1954. A Line-Formula Chemical Notation. New York: Cromwell.

Why Would I Want to Learn SMILES Notation?

The purpose of SMILES is to translate this 3-dimensional structure below, which is Morphine CAS RN 57-27-2, into a linear representation of the structure so that a computer program can understand the structure.



SMILES Notation for CAS RN 57-27-2 Oc1ccc2CC(N3C)C4C=CC(O)C5Oc1c2C45CC3

Representing Atoms

Atomic symbols and their corresponding SMILES notations:

C	methane (CH ₄)
N	ammonia (NH ₃)
O	water (H ₂ O)
P	phosphine (PH ₃)
S	hydrogen sulfide (H ₂ S)
Cl	hydrogen chloride (HCl)

Normally hydrogen is not shown.

Elements must be described in brackets:

[Au]	elemental gold
------	----------------

Representing Bonds

Single, double, triple, and aromatic bonds are represented by the following symbols:

single	-	triple	#
double	=	aromatic	:

Normally single bonds and aromatic bonds do not need to be written in the SMILES notation.

APPENDIX C: Summary of Writing SMILES Notations

SMILES: (Simplified Molecular Input Line Entry System)

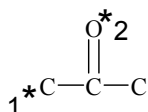
Representing Bonds (continued)

Examples showing bonds are:

CC	ethane (CH ₃ CH ₃)
C=C	ethylene (CH ₂ =CH ₂)
COC	dimethyl ether (CH ₃ OCH ₃)
CCO	ethanol (CH ₃ CH ₂ OH)
C=O	formaldehyde (CH ₂ O)
O=C=O	carbon dioxide (CO ₂)
O=CO	formic acid (HCOOH)
C#N	hydrogen cyanide (HCN)
[H][H]	molecular hydrogen (H ₂)

Bonds in Linear Structures

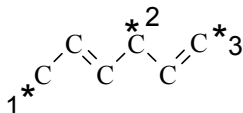
For linear structures, SMILES notation corresponds to conventional diagrammatic notation except that hydrogen can be omitted. Here are two correct ways to represent Acetone CAS RN 67-64-1. The numbered asterisks indicate where on the molecule each SMILES string begins.



valid SMILES:

1. CC(=O)C
2. O=C(C)C

Here are three correct ways to represent 1,4-hexadiene CAS RN 592-45-0. The numbered asterisks indicate where on the molecule each SMILES string begins.

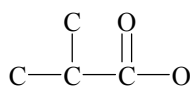


valid SMILES:

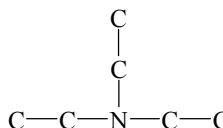
1. CC=CCC=C
2. C(C=C)C=CC
3. CC=CCC=C

Representing Branches

Branches are specified by enclosures in parentheses, for example:



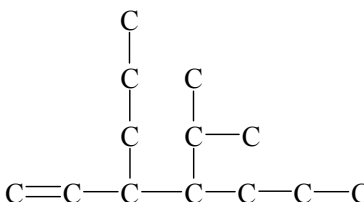
CC(C)C(=O)O
Isobutyric acid
CAS RN 79-31-2



CCN(CC)CC
Triethylamine
CAS RN 121-44-8

Branches also can be nested or stacked, for example:

C=CC(CCC)C(C(C)C)CCC
3-propyl 4-isopropyl 1-heptene

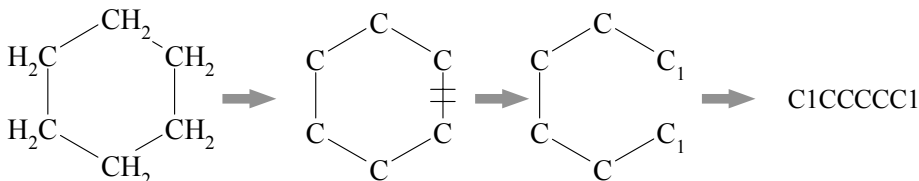


APPENDIX C: Summary of Writing SMILES Notations

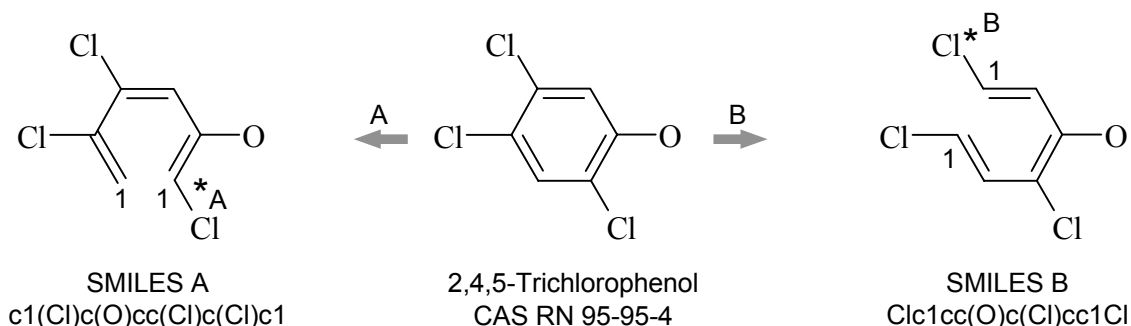
SMILES: (Simplified Molecular Input Line Entry System)

Representing Cyclic Structures

Cyclic structures are represented by breaking one single or double (aromatic) bond in each ring. The bonds are numbered in any order, designating ring-opening/closure bonds by a digit immediately following the atomic symbol at each ring closure. This leaves a connected noncyclic graph, which is written as a noncyclic structure by using the three rules described for atoms, bonds, and branches. A typical example is Cyclohexane CAS RN 110-82-7:

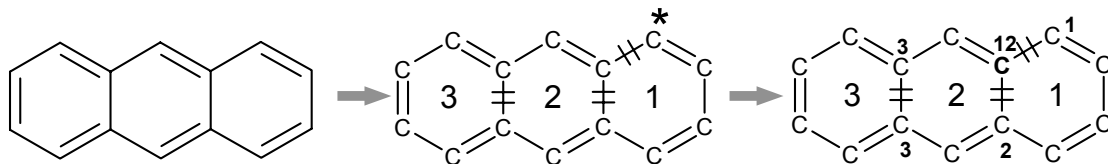


Just as in linear structures, there are many different but equally valid descriptions of the same cyclic structure. Many different SMILES notations may be written for the same structure by breaking a ring in different places. For example, here are two valid SMILES notations for 2,4,5-Trichlorophenol CAS RN 95-95-4. The numbered asterisks indicate where on the molecule each SMILES string begins.



A single atom may belong to more than one ring and have more than one ring closure. An example of this is Anthracene, in which one atom (bolded below) have more than two ring closures.

Here is the generation of the SMILES notation for Anthracene CAS RN 120-12-7. Number each ring, decide where you want to start the SMILES string (here the SMILES string will begin at the asterisk). Break the rings and give the two atoms at each ring closure the number of that ring.



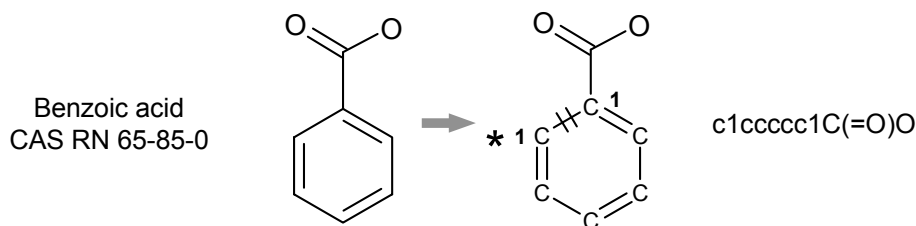
In this example the SMILES notation for Anthracene is: c1cccc2cc3ccccc3cc12

APPENDIX C: Summary of Writing SMILES Notations

SMILES: (Simplified Molecular Input Line Entry System)

Representing Cyclic Structures (continued)

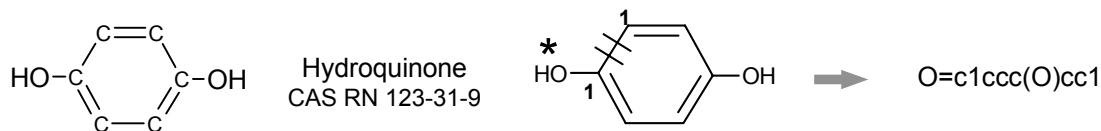
Aromatic structures are distinguished by writing the atoms in the aromatic ring in lower case letters, for example Benzoic acid CAS RN 65-85-0.



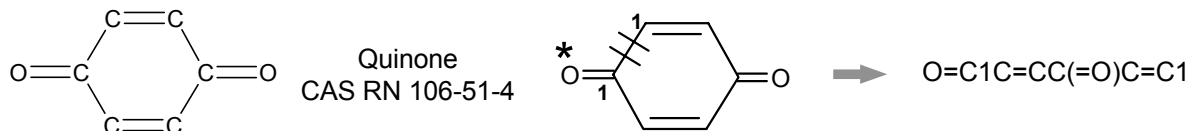
Examples of Aromatic and Nonaromatic Compounds

Of the examples shown on the previous page, Cyclohexane CAS RN 110-82-7, is not aromatic and all carbons are indicated by upper case: C1CCCCC1. Anthracene CAS RN 120-12-7 is aromatic and all carbons are indicated by lower case: c1cccc2cc3ccccc3cc12.

Hydroquinone is **aromatic**. Hydroquinone drawn with aromatic carbons shown in lower case (left) and with aromatic carbons hidden (right).

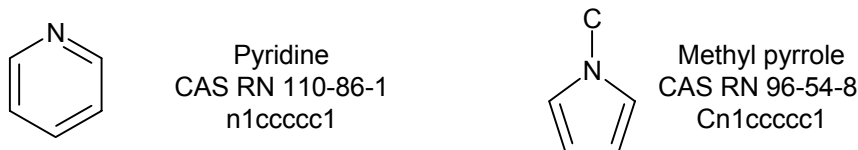


Quinone CAS RN 106-51-4 is **nonaromatic**. Quinone drawn with nonaromatic carbons shown in upper case (left) and with nonaromatic carbons hidden (right).



Aromatic Nitrogen

Aromatic nitrogens are specified with the aromatic symbol lower case "n" Examples are pyridine and pyrrole:

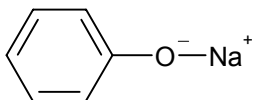


APPENDIX C: Summary of Writing SMILES Notations

SMILES: (Simplified Molecular Input Line Entry System)

Disconnected Structures

Disconnected compounds are written as individual structures separated by a period. The order in which ions or ligands are listed is arbitrary. There is no implied pairing of one charge with another, and it is not necessary to have a net charge of zero. If desired, the SMILES of one ion may be imbedded in another, as shown in the example the SMILES for Sodium phenoxide.

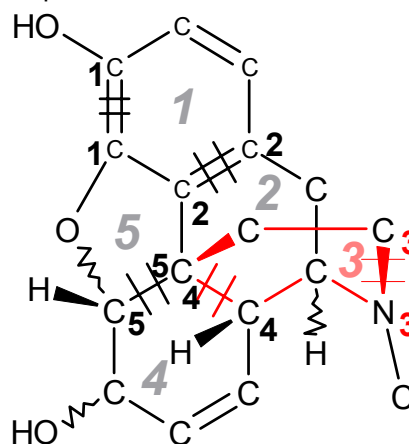
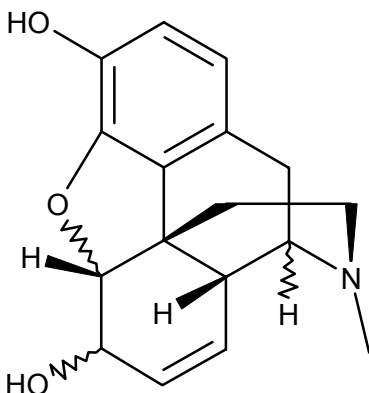


Sodium phenoxide
SMILES Notation

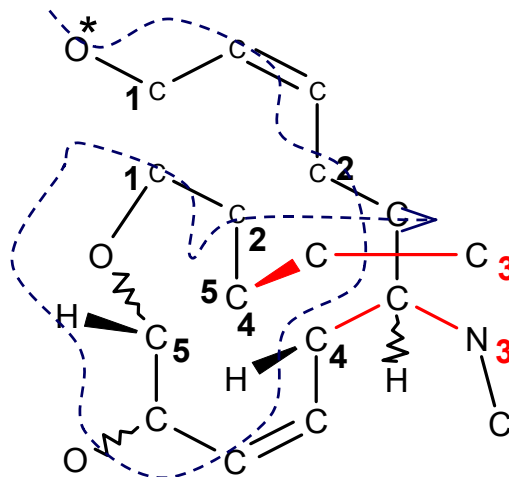
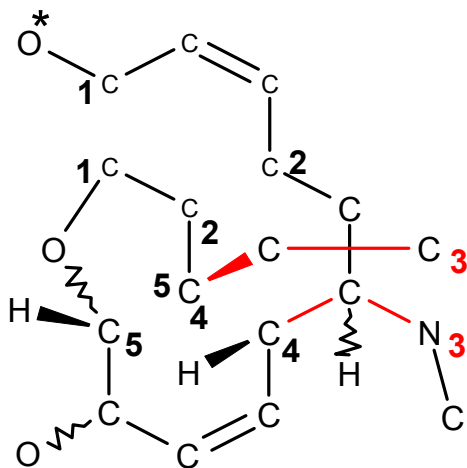
[Na+].[O-]c1ccccc1
or
c1cc([O-].[Na+])ccc1

Evolution of SMILES for Morphine

Here is the generation of one correct SMILES notation for Morphine CAS RN 57-27-2.



Number each ring, decide where you want to start the SMILES string (here the SMILES string will begin at the asterisk). Break the 5 rings and give the two atoms at each ring closure the number of that ring. The dashed line indicates the path followed when this SMILES notation was drawn.



In this example the SMILES notation for Morphine is: Oc1ccc2CC(N3C)C4C=CC(O)C5Oc1c2C45CC3

APPENDIX D: Chemicals / Characteristics Related to Local Effects

Chemicals Causing Local Effects

Note: The lists provided here are for illustrative purposes, and are not intended to be comprehensive.

Eye Effects

Chemical properties/considerations relevant to eye effects include:

- ❖ Acidity
- ❖ Basicity/alkalinity
- ❖ Chemical burns (isocyanates, mustards)
- ❖ Interaction with proteins (metal salt deposition, quinones, etc.)
- ❖ Mechanical abrasions
- ❖ Solvent effects
- ❖ Surfactancy

Toxicity/irritation/corrosion to the Skin

Irritation Consider:

- ❖ Acidity
- ❖ Basicity/alkalinity
- ❖ Chemical burns
- ❖ Lipophilicity
- ❖ Mechanical abrasions
- ❖ Solvent effects
- ❖ Surfactancy

Dermal/Contact Sensitization Consider:

- ❖ Electrophilic or nucleophilic groups that could haptenize protein through covalent modification, for example: Aldehydes, ketone, codicils, quinones, other conjugated, unsaturated functional groups, epoxy groups.
- ❖ Structural similarities to classes of contact allergens (parent chemical) or impurities belonging to known classes of contact allergens, for example: Antibiotics, Chlorinated antiseptics, Dyes (azo, amine), Formaldehyde releasers, Mercurials, Metals (nickel, chromium, cobalt), Natural products (plant rosins, balsams), and Preservatives.

Photo-toxicity and Photosensitization Consider:

- ❖ Chemical structures that are UV absorbing (such as highly conjugated aromatics), for example: Furocoumarins, Polycyclic aromatics, and Porphyrins.
- ❖ Structural similarity to systemic agents that cause photoreactions, for example: Non-steroidal anti-inflammatory agents, Sulfonamides, and Tetracyclines.

Local Toxicity to the Gastrointestinal Mucosa Consider:

- ❖ Local effects in the G.I. tract will be mediated by solubility, irritation, corrosivity, and local metabolism.
- ❖ For irritant and corrosive effects, consider the factors elaborated above for eye and skin.
- ❖ For metabolic activation, consider the factors elaborated upon below.

Toxicity to the Respiratory System Consider:

- ❖ Irritants that may cause asthma, a disease characterized by (1) airway obstruction that is reversible, (2) airway inflammation, and (3) airway hyperresponsiveness. Classes of compounds that can cause asthma include: Aldehydes, Anhydrides, Isocyanates, and Metals.
- ❖ Irritant materials may cause upper airway reactivity (e.g., bronchitis)
- ❖ Water soluble, reactive materials (e.g., formaldehyde) may cause nasal or upper airway toxicity an/or irritation
- ❖ Particulates and fibers of a particle size that results in deep lung deposition may potentially cause chronic lung injury. Such injury is mediated by inflammatory responses, lung overload, and sustained cell turnover. Examples include: Fibers with a certain length to width ratio (e.g., asbestos), and Particulate dusts (silica, clays, talcs).
- ❖ Other classes of respiratory toxicants include: Ammonia and volatile, basic amines, Isocyanates, Metal carbides, Metal oxides, Metal dusts and fumes, Nitrogen oxides, Surfactants, and Transition metals, arsenic, beryllium.

APPENDIX E: Chemicals Causing Systemic Effects

Systemic Toxicity Mediated by Intrinsic Chemical Reactivity or Biotransformation to Reactive Toxicants

Systemic organ toxicity is frequently mediated by the presence of reactive functional groups (whether present in the parent compound or introduced via biotransformation). Reactive compounds or metabolites may exert toxic effects by modification of cellular macromolecules (structural and functional cellular proteins, DNA). This can result in destruction or dysfunction of the target molecules. In addition, covalent modification of target molecules which are covalently modified may render them "foreign" or antigenic (capable of eliciting an immune response). DNA-reactive chemicals have genotoxic potential.

Toxicity Caused by Electrophiles Structural "Red flags" for chemicals containing electrophilic centers include:

- ❖ Acyl halides
- ❖ Aryl halides
- ❖ Azides, – and S-mustards
- ❖ Epoxides, strained rings (e.g., sultones)
- ❖ Nitroso groups
- ❖ Polarized, conjugated double bonds (e.g., quinones, α , β unsaturated ketones, esters, nitriles)

Functional groups which undergo metabolism to electrophilic centers include:

- ❖ Alkyl esters of sulfonic or phosphonic acids
- ❖ Aromatic compounds with functional groups that can yield benzylic, aryl carbonium or Nitronium ions
- ❖ Aromatic nitro, azo or amine groups
- ❖ Conjugated aromatics that undergo epoxidation

Toxicity Caused by Free Radical Formation Compounds which can accept or lose electrons can mediate free radical formation through redox cycling. Structural "Red flags" include:

- ❖ Aminophenols
- ❖ Catechols, quinines, hydroquinones
- ❖ Metal complexes (iron and chromium)
- ❖ Peroxides
- ❖ Phenothiazines
- ❖ Polycyclic aromatics

Systemic Toxicity Associated with Receptor-Mediated Mechanisms Some compounds exert toxicity through substitution for known or unknown tissue receptor ligands. Classes of compounds that could exert toxicity through such mechanisms include:

- ❖ Environmental estrogens (putative hormone receptor ligands)
- ❖ Fibrates, phthalates (peroxisome proliferator receptor agonists)
- ❖ Polychlorinated aromatics (Ah receptor ligands)
- ❖ Retinoids (retinoic acid receptor ligands)

Target Organ and Functional Toxicity

Toxicity to the Liver As the primary organ of biotransformation, the liver is susceptible to toxicity mediated by chemical reactivity, as described above. Other agents with toxicity to the liver include:

- ❖ Chlorinated hydrocarbons
- ❖ Metals, etc.

APPENDIX E: Chemicals Causing Systemic Effects

Toxicity to the Kidney Classes of compounds that are potential nephrotoxins include:

- ❖ Amines
- ❖ Certain classes of systemic drugs
- ❖ Halogenated aliphatic hydrocarbons
- ❖ Heavy metals
- ❖ Herbicides
- ❖ Insoluble salts that precipitate in the kidney (e.g., calcium complexes)
- ❖ Mycotoxins
- ❖ Organic solvents

Toxicity to the Respiratory System Effects of inhaled respiratory toxicants were addressed above.

Neurotoxicity Chemicals/Classes of compounds which may manifest neurotoxicity include:

- ❖ Acids and thioacids
- ❖ Arylamide and related substances
- ❖ Acrylamides
- ❖ Alcohols
- ❖ Aliphatic halogenated hydrocarbons
- ❖ Alkanes
- ❖ Aromatic hydrocarbons
- ❖ Carbon disulfide and organic sulfur -containing compounds
- ❖ Carbon monoxide
- ❖ Catecholamines
- ❖ Certain classes of systemic drugs
- ❖ Chlorinated solvents
- ❖ Cyanide
- ❖ Cyclic halogenated hydrocarbons
- ❖ Environmental estrogens
- ❖ Ethylene oxide
- ❖ Gamma-diketones
- ❖ Inorganic nitrogenous compounds
- ❖ Isocyanates
- ❖ Ketones
- ❖ Lead
- ❖ Mercury compounds
- ❖ Metals and metalloids other than mercury and lead
- ❖ Nitriles
- ❖ Organic nitrogens
- ❖ Organophosphates
- ❖ Organophosphorus compounds
- ❖ Organotins
- ❖ Certain Pesticides
- ❖ Phenols and related substances
- ❖ Phosphorus
- ❖ Protein cross-linking agents
- ❖ Psychoactive drugs
- ❖ Pyridines (e.g., MPTP)

APPENDIX E: Chemicals Causing Systemic Effects

Immunotoxicity (Immunosuppression / Autoimmunity) Classes of compounds which may manifest immunotoxicity include:

- ❖ Heavy metals
- ❖ Organic solvents
- ❖ Certain Pesticides
- ❖ Polyhalogenated aromatic hydrocarbons

Genetic Toxicity Classes of compounds that manifest genetic toxicity are often electrophilic agents capable of modifying DNA. Such agents may act as gene mutagens, clastogens or aneugens. Compounds that can intercalate into DNA, free radical generators or chemicals that induce oxidative damage may also act as gene mutagens, clastogens or aneugens.

Mutagenic structural alerts include:

- ❖ Acrylates and methacrylates
- ❖ Aliphatic or aromatic nitro groups
- ❖ Aliphatic or aromatic epoxides
- ❖ Alkyl hydrazines
- ❖ Alkyl esters of phosphonic or sulfonic acids
- ❖ Alkyl aldehydes
- ❖ Aromatic ring N-oxides
- ❖ Aromatic azo groups
- ❖ Aromatic and aliphatic aziridynyl derivatives
- ❖ Aromatic alkyl amino or dialkyl amino groups
- ❖ Aromatic and aliphatic substituted alkyl halides
- ❖ Aromatic amines and N-hydroesters of aromatic amines
- ❖ Carbamates
- ❖ Chloramines
- ❖ Halomethanes
- ❖ Monohaloalkanes
- ❖ Multiple-ring systems
- ❖ N-methylol derivatives
- ❖ Nitrogen and sulfur mustards
- ❖ Nitroso compounds
- ❖ Propiolactones and propiosultones
- ❖ Vinyls and vinyl sulfones

Reproductive Toxicity Classes of compounds which may manifest reproductive toxicity include:

- ❖ Alcohols
- ❖ Alkylating agents
- ❖ Chlorinated hydrocarbons
- ❖ Certain Fungicides
- ❖ Certain Herbicides
- ❖ Hydrazines
- ❖ Certain Insecticides
- ❖ Metals and trace elements
- ❖ Nonylphenols
- ❖ Plastic monomers
- ❖ Solvents (e.g., glycol ethers, benzene, xylenes)
- ❖ Steroids or steroid receptor ligands

APPENDIX E: Chemicals Causing Systemic Effects

Developmental Toxicity Classes of compounds which may manifest developmental toxicity include:

- ❖ Acrylates
- ❖ Androgenic chemicals
- ❖ Anilines
- ❖ Boron containing compounds
- ❖ Chelators
- ❖ Chlorobiphenyls
- ❖ Compounds which have potential for mutagenicity and oncogenicity
- ❖ Epoxides
- ❖ Lead
- ❖ Lithium
- ❖ Mercury
- ❖ Nitrogen Heterocyclic compounds
- ❖ Phthalates
- ❖ Retinoids
- ❖ Salicylates
- ❖ Short-chain branched carboxylic acid (e.g., valproic acid)
- ❖ Small benzenes
- ❖ Synthetic steroids (e.g., diethylstilbestrol)
- ❖ Triazines
- ❖ Vinyl groups

Blood Toxicity Classes of compounds which may manifest developmental toxicity include:

- ❖ Simple aromatic amines and azo dyes that undergo azo reduction to release aromatic amines

APPENDIX F: High Molecular Weight Polymers

High Molecular Weight Polymers in the New Chemicals Program

From: <http://www.epa.gov/opptintr/newchems/hmwtpoly.htm> August 2002

There are three categories or types of High Molecular Weight (HMW, >10,000 daltons) polymers typically reviewed by EPA's New Chemicals Program: (a) soluble, (b) insoluble/non-water absorbing ("non-swellable"), and (c) water absorbing ("swellable"). EPA has a concern for potential fibrosis of the lung or other pulmonary effects that may be caused by inhalation of respirable particles of water-insoluble HMW polymers. The toxicity may be a result of "overloading" the clearance mechanisms of the lung. EPA also has concerns for water absorbing polymers, based on data showing that cancer was observed in a 2-year inhalation study in rats on a HMW water-absorbing polyacrylate polymer. Each of the three types is treated differently as indicated below:

a. Soluble. EPA does not expect water-soluble polymers to exhibit lung toxicity because they are expected to rapidly clear the respiratory tract and therefore not cause an overloading effect. However, where there is substantial production volume, exposure and release, the Agency will require testing on PMN substances of this type under its exposure-based authority.

b(1). Insoluble: non-water swellable. Although exempt from reporting by the 1995 PMN rule amendments under the polymer exemption criteria, the Agency has concerns for this class of HMW polymers. This concern is based on a study, designated TSCA 8(e)-0668, which reported irreversible lung damage linked with inhalation of respirable particles of water-insoluble polymers (toner used in copy machines) of MW 70,000 or greater. There is a data gap for polymers with MW between 10,000 and 70,000. If a company chooses to submit a PMN for this type of HMW polymer (rather than take advantage of the polymer exemption option), and the PMN substance meets the program's exposure-based criteria (in particular, production volume and inhalation exposure), EPA may regulate under its exposure-based policy with a modified testing scheme. A 90-day subchronic toxicity test via inhalation with a 60-day holding period (absent neurotoxic components and other organ effects) will be triggered under a TSCA Section 5(e) consent order. Data from such a study will be compared to results from 8(e)-0668.

Other references are:

A. Pulmonary Response to Toner Upon Chronic Inhalation Exposure in Rats. H. Muhle, B. Bellmann, O. Creutzenberg, C. Dasenbrock, H. Ernst, R. Kilpper, J.C. MacKenzie, P. Morrow, U. Mohr, S. Takenaka, and R. Mermelstein. *Fundam. Appl. Toxicol.* 17, 280-299(1991).

B. Lung Clearance and Retention of Toner, Utilizing a Tracer Technique During a Long-term Inhalation Study in Rats. B. Bellmann, H. Muhle, O. Creutzenberg, C. Dasenbrock, R. Kilpper, J.C. MacKenzie, P. Morrow, and R. Mermelstein. *Fundam. Appl. Toxicol.* 17, 300-313(1991).

C. Chronic Inhalation Study Findings as a Basis for Proposing a New Occupational Dust Exposure Limit. P. Morrow, H. Muhle, and R. Mermelstein. *J. American College of Toxicology*, 10, No. 2, 279-290(1991).

D. Abstract-Hamster Response to Chronic Test Toner Inhalation. R. Mermelstein, O. Creutzenberg, C. Dasenbrock, H. Ernst, M. Kushner, U. Mohr, and H. Muhle. presented at the 1992 Annual Society of Toxicology (SOT) Meeting, Seattle, WA, *The Toxicologist* (1992).

b(2). Insoluble: non-water swellable, highly respirable. Also exempt from reporting under the new polymer exemption. In addition to lung overload described above, these substances raise serious, yet less predictive concerns for potential lung effects associated with their highly respirable size--where a significant percentage of the particles are <10 microns--and lack of absorption potential; the physical effect is deposition to the deep lung and inability to dislodge the particles. For these cases, current Agency policy is to not pursue regulation of the chemical, but to send a letter to the submitter that mentions the basic overload issue from above--with the toner data references--and stresses the heightened concern based on the substance's highly respirable nature--with additional references on "ultrafines," highly respirable particles that are much more toxic to lungs than larger particles of the same material. Such a letter typically will recommend use of a NIOSH-approved respirator or appropriate engineering controls.

APPENDIX F: High Molecular Weight Polymers

General Note on the Insoluble HMW Polymers and the Polymer Exemption. EPA recognizes that there is a different hurdle for placing PMN chemical substances on the TSCA (Toxic Substances Control Act) Inventory than for permitting exemptions for polymers, specified at 40 CFR 723.250. In promulgating this exemption for polymers, EPA generally concluded that "there is an exceedingly low probability that potential exposure to high molecular weight water-insoluble polymers, as a class, will result in unreasonable risk or injury to human health or the environment." (see 60 FR 16322; March 29, 1995). Within the context of individual PMN chemical substances, however, EPA continues to have a concern for the potential for irreversible lung damage when respirable insoluble dusts are inhaled at levels that also produce "lung overloading" and impaired clearance by the lungs. As a result, EPA will assess polymers submitted as PMNs on a case-by-case basis. This concern is based on the above mentioned photocopy toner data (TSCA 8(e)-0668). Based on this concern, EPA reserves the right to require testing under its TSCA exposure-based authority, warranted by high exposures and production volume. In promulgating the polymer exemption in 40 CFR 723.250, EPA did not impose conditions on this category of insoluble high MW polymers as part of the final rule. At the time, EPA stated that, "the Agency believes that manufacturers and users of polymers and chemical substances, in general, where feasible should take appropriate action to mitigate exposure to all respirable particles as part of good industrial hygiene practices." (See 60 FR 16323; March 29, 1995). Accordingly, EPA may send a "letter of concern" to a PMN submitter, as a restatement of this last point. EPA believes such a letter is an appropriate action which fulfills EPA's responsibility to communicate a potential for adverse effects based on the TSCA Section 8(e) photocopy toner data. Note that EPA, in promulgating the 1995 amendments to the Polymer Exemption Rule, elected not to establish an exposure limit for respirable particles, agreeing with public comments that consistency among Federal regulations (i.e., between TSCA new chemicals regulation and OSHA nuisance dust standards) regarding workplace exposure is desirable.

c. Water absorbing (swellable) polymers. For these substances the Agency makes the "may present an unreasonable risk" determination with concerns for fibrosis and cancer, based upon water absorption properties. Concerns are associated with substances that absorb their weight (or greater) in water. The primary reference for Agency concerns for this class of polymers is TSCA 8(e)-1795, submitted by the Institute for Polyacrylate Absorbents (IPA), which indicated that high molecular weight polyacrylate polymers caused lung neoplasms in animal studies. EPA has also reviewed data on modified starches submitted by the Corn Refiners Association, comparing the structures of the test substances with the structures of twelve modified starch PMN substances. You can view the tea-bag protocol (22 Kb PDF) used for this study. Based on the submitted data, EPA was unable to support concerns for the water retentive capacity of these PMN substances as potentially leading to lung cancer. EPA will review future PMNs for modified starches on a case-by-case basis to determine the applicability of these test results to the future PMNs. High molecular weight polymers that swell to twice their weight are not eligible for the polymer exemption. EPA will assess on a case-by-case basis whether these substances pose a risk and whether testing is warranted, and if they are made in substantial amounts and demonstrate potential for acute or chronic worker inhalation exposure.